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## Leading technology for in vivo fluorescent sarcoma imaging

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**Background:** Naturally fluorescent proteins have revolutionized biology by enabling what was formerly invisible to be seen clearly. The green fluorescent protein (GFP) gene is frequently used as a reporter of expression and a biosensor in living animals. However, in orthopedic research, fluorescent proteins have only been used in a limited fashion. We have developed fluorescent real-time imaging for sarcoma cells by means of multi-color fluorescent cell lines and transgenic mice. **Methods:** Sarcoma cells were labeled with GFP or red fluorescent protein (RFP). Color-coded cells were transplanted into bone, spinal cord, or lung and their dynamics were observed in live mice. Transgenic mice were also used as the host in which GFP was driven by a stem cell marker nestin. Nascent blood vessels and immature neurons expressed GFP in this model. Indocyanine green was injected into tumor bearing mice to visualize tumor mass and peritumoral vascular structure. **Results:** Fluorescence imaging readily distinguished the color-coded cell lines and their differential ability to survive at the primary sites as well as metastasizing in live mice. Imaging of sarcoma cell trafficking in vessels revealed critical steps of metastasis. In transgenic mice, nascent blood vessels in the growing tumors were visualized. Lung metastasis was observed directly under fluorescent light and a large number of cells were arrested but the cell number decreased rapidly at 24 hours. Single disseminated cells tended to die earlier than cells in aggregates. Dual colored fibrosarcoma cells were also injected into either the portal vein or abdominal aorta in nude mice. The liver and muscle were imaged to visualize the fate of the cells. The rate of sarcoma cell death was highest in the lung and lowest in the muscle. In each organ, single disseminated cells tended to die earlier than aggregated cells. Indocyanine green can image tumor angiogenesis and peritumoral lymphatic channels. This technology can be utilized fluorescent guided surgery, such as tumor imaging, avoiding vascular injuries and sentinel lymph node biopsy. **Conclusion:** Real time in vivo imaging of sarcoma cells enabled visualization of their dynamics, including cell mobility, invasion, metastasis and angiogenesis.

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## **p53-mediated apoptosis induction attenuates the resistance to oncolytic adenovirus in human osteosarcoma cells**

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**Background:** We recently revealed that a telomerase-specific replication-competent oncolytic adenovirus, OBP-301, shows the cytopathic activity in human bone and soft tissue sarcoma cells. However, some human osteosarcoma cells were less susceptible to OBP-301. In this study, we generated OBP-702, in which a human wild-type p53 gene expression cassette was inserted into the E3 region of OBP-301, and compared the antitumor effects between OBP-702 and OBP-301 in OBP-301-sensitive and OBP-301-resistant human osteosarcoma cells.

**Methods:** We used three OBP-301-sensitive (U2OS, OST, HOS) and two OBP-301-resistant (SaOS-2, MNNG/HOS) human osteosarcoma cells. The difference of cytopathic activity between OBP-702 and OBP-301 was analyzed using XTT assay. The 50% inhibiting dose (ID50) value of OBP-702 and OBP-301 for each cell line was calculated using cell viability data obtained on day 5 after virus infection. Induction of apoptosis was assessed in OBP-301-resistant osteosarcoma cells infected with OBP-702, OBP-301 or Ad-p53, which is a p53-expressing replication-deficient adenovirus, by FACS analysis measuring active caspase-3 expression. The expressions of p53, p21 and cleaved PARP proteins were evaluated using western blot analysis. The in vivo antitumor effect of OBP-702, OBP-301 and Ad-p53 was studied using orthotopic human osteosarcoma MNNG/HOS tumor model with total three intratumoral injections every 2 days.

**Results:** OBP-702 showed more cytopathic activity than OBP-301 in both OBP-301-sensitive and OBP-301-resistant osteosarcoma cells. The ID50 value of OBP-702 was lower than that of OBP-301 in all cell lines. FACS analysis demonstrated that OBP-702 significantly increased active caspase-3 compared with Ad-p53 and OBP-301. OBP-702 induced higher expression of p53 and cleaved PARP than Ad-p53. However, p21 up-regulation was not observed in SaOS-2 and MNNG/HOS cells infected with OBP-702. These results suggested that OBP-702 could efficiently induce apoptosis in OBP-301-resistant osteosarcoma cells. In vivo intratumoral injection of OBP-702 significantly suppressed tumor growth compared with OBP-301, Ad-p53 and PBS using MNNG/HOS tumor xenograft model.

**Conclusion:** OBP-702 mediated p53 gene transduction remarkably induces apoptosis, resulting in the enhancement of antitumor effect. OBP-702 would be a promising treatment modality for patients with osteosarcoma.

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## Studies of Osteosarcoma Metastasis Driver Genes using Transposon Mutagenesis in Mice and TALEN-Mediated Gene Knockouts in Osteosarcoma Cell Lines

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**Background:** Random insertion of Sleeping Beauty (SB) transposons in somatic cells produces mutations leading to tumor development, which has successfully identified candidate genes for many types of cancer.

**Methods:** We created transgenic mice that develop osteosarcoma (OS) via SB transposon-mediated mutagenesis activated by an osteoblast specific Osterix-cre recombinase transgene (Osx-Cre). Tumorigenesis was accelerated with a Trp53 pathway deficient background (Trp53R270H/+). Ligation-mediated PCR, next generation DNA sequencing, and TAPDANCE software identified recurrent transposon sites in DNA isolated from primary tumors and metastatic nodules. Using transposon integration sites as molecular tags, non-supervised hierarchical clustering analysis assessed relatedness among metastatic and primary tumor sets. Copy number variation of candidate genes was evaluated in human matched normal, primary and metastases OS samples.

**Results:** Our quadruple transgenic mice (Osx-Cre; R26-LSL-SB11; LSL-Trp53R270H; T2/Onc) develop OS with an average latency of 10.5 months and a penetrance of 75% (n=96), compared to 17 months and 60% (n=49) in Trp53R270H/+ controls. SB tumors resemble human OS in gross anatomy, histological appearance, and presence of collagen. Over 100 metastatic nodules were collected from 16 quadruple transgenic mice. Analysis of recurrent SB integration sites revealed the well-known OS genes RB1 and CMYC in primary tumors, validating the screen, and novel genes not previously reported, including 10 genes common among metastatic nodules. Metastases from the same mice were clonal derivatives from the primary tumor and generally more related to each other than to the primary tumor, even when collected from different organs. Many of the genes identified by the SB screen mapped to regions with copy number changes in human OS tumors.

**Conclusion:** The SB screen revealed high clonality among metastases and identified several candidate metastatic drivers. Functional validation using published in vitro assays for migration and invasion is being conducted on cell lines derived from lung and primary tumor pairs collected from the SB mice and well-characterized human and murine OS cell lines: U2OS, HOS, MNNG/HOS, 143B, K12, and K7M2. Gene expression will be increased using over expression vectors containing cDNA and/ or silenced using transcription activator-like effector nuclease (TALENs) mediated gene knockout.

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## Prospective identification of tumorigenic sarcoma cancer stem cells based on high aldehyde dehydrogenase 1 activity

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Tumors contain a small population of cancer stem cells (CSC) proposed to be responsible for tumor maintenance and relapse. Aldehyde dehydrogenase 1 (ALDH1) activity has been used as a functional stem cell marker to isolate CSCs in different cancer types. This study used the Aldefluor® assay and fluorescence-activated cell sorting (FACS) analysis to isolate ALDH1<sup>high</sup> cells from five human sarcoma cell lines and one primary chordoma cell line. ALDH1<sup>high</sup> cells range from 0.3% (MUG-Chor1) to 4.1% (SW-1353) of gated cells. Immunohistochemical staining, analysis of the clone formation efficiency, and xCELLigence microelectronic sensor technology revealed that ALDH1<sup>high</sup> cells from all sarcoma cell lines have an increased proliferation rate compared to ALDH1<sup>low</sup> cells. By investigating of important regulators of stem cell biology, real-time RT-PCR data showed an increased expression of c-Myc,  $\beta$ -catenin, and SOX-2 in the ALDH1<sup>high</sup> population and a significant higher level of ABCG2. Statistical analysis of data demonstrated that ALDH1<sup>high</sup> cells of SW-982 and SW-1353 showed higher resistance to commonly used chemotherapeutic agents like doxorubicin, epirubicin, and cisplatin than ALDH1<sup>low</sup> cells. Using a NOD/SCID mice xenograft model, ALDH1<sup>high</sup> cells showed a greater tumor forming capacity compared to ALDH1<sup>low</sup> cells. The ALDH1<sup>high</sup> tumors were significantly larger than the ALDH1<sup>low</sup> tumors after 4-6 weeks.

This study demonstrates that in different sarcoma cell lines, high ALDH1 activity can be used to identify a subpopulation of cells characterized by a significantly higher proliferation rate, increased colony forming, increased expression of ABC transporter genes and stemness markers compared to control cells. In addition, enhanced drug resistance and a greater tumor forming capacity were demonstrated.

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## Sesquiterpene lactones affect G2/M cell cycle arrest and apoptosis in human soft tissue sarcoma cell lines

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Uncontrolled proliferation, metastasis and failure in apoptosis constitute crucial elements in the development and progression of tumors. Several studies have demonstrated the efficacy of plant-derived agents in the treatment of various malignant entities. The present study investigated the anti-tumor effects of costunolide and dehydrocostus lactone isolated from *Saussurea lappa* in three human soft tissue sarcoma (STS) cell lines of various origins.

Cell proliferation was determined using the MTS assay and xCELLigence technology. Cell cycle distribution, cleaved caspase-3, and Annexin V/PI were analysed by FACS analysis. The protein expression level of PARP and cleaved-PARP, G1- and G2/M cell cycle checkpoints were analysed using western blotting.

Both compounds inhibited cell proliferation of STS cell lines at concentrations ranging from 0.5 to 100 µg/ml and incubation periods from 24 to 72 h. After costunolide treatment, no significant changes in cell cycle distribution were detected compared to untreated control groups. However, dehydrocostus lactone caused a significant reduction of the G1 phase and an increase in S and G2/M phases, as well as high levels of cleaved caspase-3 and PARP cleavage. The expression levels of CDK2, CDK1 (cdc2), cyclin B1, and p27 decreased significantly after dehydrocostus lactone treatment in a dose-dependent manner. Thus, G2/M arrest via the CDK1 down-regulation may be an important molecular mechanism by which dehydrocostus lactone inhibits cancer cell growth.

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## Histone deacetylase inhibitors as potential therapeutic targets for chordomas: an immunohistochemical and functional analysis

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**Introduction:** Chordomas are rare malignancies of the axial skeleton. Therapeutic modalities are mainly restricted to surgery and irradiation. HDAC inhibitors are tested in many clinical trials as promising new treatment options for various types of cancer.

**Objectives:** We intended to study whether HDAC inhibitors could be regarded as therapeutic targets for chordomas.

**Materials and Methods:** Fifty chordomas (34 primary tumors, 16 recurrences) from 44 patients (27 male, 17 females) were evaluated immunohistochemically for the expression of HDACs1-6. HDAC inhibitors Vorinostat (SAHA), Panobinostat (LBH-589), and Belinostat (PXD101) were tested in the chordoma cell line MUG\_Chor1 for dose-dependent apoptotic effects. Apoptosis induction was investigated by caspase 3/7 activity, caspase-3 cleavage and PARP cleavage. P-values > 0.05 were considered significant.

**Results:** IHC: HDAC1 expressed a slight nuclear positivity (n = 5; 10%). Expression of HDAC2 was positive in the majority of cases (n = 36; 72%). HDACs 3 to 6 stained positive in all specimens available (n = 43; 86%). The strongest expression was observed for HDAC6.

**Cell line:** Caspase 3/7 activity was measured by the Caspase-Glo® 3/7 Assay in MUG-Chor1 cells after 3, 6, 24, 48, and 72 h treatment with the IC50 of SAHA, LBH-589, and PXD101. It peaked after 48 and 72 h in SAHA and LBH-589 treated cells. PXD101 treatment did not lead to caspase 3/7 activity. Cleaved caspase-3 was detected in 54.5±7.4% of SAHA treated, and in 63.1±13.2% of LBH-589 treated cells. In contrast, the control and PXD101 treated cells showed almost no cleaved caspase-3 (2.7±1.5% and 8.2±3.4% of gated cells, respectively). The percentage of cleaved caspase-3 positive cells increased significantly over time (p=0.0003 for SAHA, and p=0.0014 for LBH-589 after 72h).

**Discussion:** HDACs were detectable by IHC in our series, with HDAC1 showing the weakest, and HDAC6 showing the strongest staining. SAHA and LBH-589 significantly increased apoptosis of chordoma cells. Although sufficient data from chordomas is still lacking, the efficacy of various HDAC inhibitors has been shown in several types of sarcomas, particularly in combination with other anticancer therapeutics. Our results provide evidence to support further research on HDACs as potential therapeutic targets for chordoma therapy.

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## Gene expression of extracellular matrix proteins in lung metastases of giant cell tumour of bone: tumour or location specific?

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### BACKGROUND

Giant cell tumour of bone (GCTB) is a primary bone tumour with an unpredictable clinical behavior which could sometimes be worrisome. One of these features is its ability to metastasize to the lungs. The mechanisms of this phenomenon have not been well understood. Recent studies indicate that the extracellular matrix may play a pivotal role in the primary tumor location to enhance its metastatic potential. Three of these reported genes are lumican (LUM), decorin (DCN) and tenascin which are all involved in the delicate balance between mobility and crosslinking of diverse components in the extracellular matrix.

### AIMS

To investigate whether the expression of two of these ECM components - LUM and DCN as an example - are truly location specific (lung vs. bone) or tumour specific (metastasis and its primary tumour vs. non-metastasizing tumours).

### METHODS

In total 31 samples of GCTB were used (5 primary, 6 lung-metastatic and 20 non-metastasizing GCTB samples). RNA extraction with cDNA synthesis and qPCR was performed in duplicate. Reference genes were selected and primers were designed against Lumican and Decorin using Primer-Blast, Oligo7 and mFold. The data were analyzed and using qBaseplus (Biogazelle). Statistical analyses were performed using the unpaired and paired t-test.

### RESULTS

Comparison of the different gene expression profiles of LUM and DCN in the different GCTB-groups exhibits following results:

- no significant differential gene expression between lung meta's and their primary located tumours (DCN:  $p < 0,804$ . LUM:  $p < 0,283$ ).
- A significant lower differential gene expression in the lung meta's compared to the non-metastasizing tumour samples (DCN:  $p < 0,002$ . LUM:  $p < 0,001$ )
- A significant lower differential gene expression of the metastasizing primary tumours when compared to the non-metastasizing tumour (DCN:  $p < 0,003$ . LUM:  $p < 0,001$ ).

### CONCLUSION

As the gene expression of both extracellular matrix proteins differs significantly between meta's and non-metastasizing tumours and between primary tumours compared with the non-metastasizing groups, proves that the expression of LUM and DCN is tumour specific. Moreover, a lower differential gene expression of these ECM genes is a potential indicator and therefore an alarm for those tumours at risk to metastasize.

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## Possible roles of osteosarcoma-derived exosomes in promoting pre-metastatic niche in the lung

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### Background

Recent studies have shown the involvement of tumor-derived exosomes in tumor progression. Exosomes are nanometer-sized vesicles secreted by diverse cell types that play complex roles in intercellular communication. They comprise a ceramide- and cholesterol-rich lipid bilayer membrane, and contain both mRNA and microRNA, which can be delivered to another cells. Furthermore, neutral sphingomyelinase 2 (nSMase2), regulating the biogenesis of ceramide, were found to trigger secretion of exosomes. In this study, we investigated the role of OS-derived exosomes in lung metastasis through the regulation of ceramide signaling pathway.

### Methods

We used a highly metastatic human OS cell line 143B cells expressing firefly luciferase (143B F-luc) and established a derivative cell line with shRNA knockdown of neutral sphingomyelinase 2 (143B-F luc-KD-nSMase2). Exosomes derived from 143B F-luc were isolated by ultracentrifugation. Original 143B F-luc cells were orthotopically transplanted to the right tibia of nude mice at  $1.5 \times 10^6$  cells/mouse (group 1). Mice similarly transplanted with 143B-F-luc-KD-nSMase2 cells were divided into 2 groups, and were intravenously administered 200  $\mu$ L PBS (group 2) or 5  $\mu$ g-exosomes/200  $\mu$ L PBS (group 3) twice a week for 3 weeks. Lung metastases were monitored by IVIS system.

### Results

Lung metastases were observed in 7/10 mice in group 1 at 3 weeks after orthotopic transplantation. In contrast, only 3/10 mice showed lung metastases in group 2, indicating the decreased metastases following the inhibition of exosome secretion. Remarkably, however, 7/10 mice showed metastases in group 3, indicating that systemically administered exosomes restored the metastatic ability. Histopathological examination of the lungs confirmed that the numbers of metastatic foci were dramatically reduced in group 2 compared with group 1, whereas that in group 3 was comparable to group 1.

### Conclusion

We demonstrated that exosomes secreted by highly metastatic osteosarcoma cell line into the circulation promoted lung metastasis *in vivo*. Given the accessibility of exosomes to distant organs, we hypothesize roles of exosomes in pre-metastatic niche formation in the lung, and are now exploring the underlying molecular mechanisms.

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## Insulin-like growth factors (IGF) I and II, and IGF binding proteins 1, 3 levels in bone tumor patients blood serum

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**Objectives:** Bone tumors are a group of musculo-skeletal diseases that are extremely difficult to diagnose. The difficulty of biopsy and a large percent of non-informative punctures impose necessity to introduce serum biomarkers determination in patients with bone neoplasms for facilitating diagnostics. The objective of this study was to measure some insuline-like growth factor system components in blood serum of malignant and benign bone tumor patients and practically healthy persons in order to assess their associations with the key tumor characteristics.

**Methods:** 162 persons aged 14 - 69 years were involved in the study: 113 bone tumor patients (25 with osteogenic sarcoma, 21 - chondrosarcoma, 18 Ewing sarcoma, 5 - malignant fibrous histiocytoma, 14 - giant cell bone tumor, and 30 with various benign tumors) and 49 practically healthy people as a control. IGF-I, IGF-II, IGFBP-1, and IGFBP-3 levels were measured in blood serum with standard ELISA Assay Kits (DSL Inc, USA).

**Results:** Serum IGF-I levels were significantly higher in patients with malignant bone tumors than in those with benign lesions, and IGF-I level in benign bone tumor patients sera was significantly higher than in control group. Serum IGF-II in malignant bone tumor patients was higher than in both benign bone tumor patients, and control persons. Serum IGF-I in patients with chondrosarcoma was significantly lower than in Ewing sarcoma and osteogenic sarcoma groups. IGFBP-1 levels did not differ between the whole group of bone tumor patients and controls. And serum IGFBP-3 was the highest in benign bone tumor patients, lower in patients with malignant tumors, and the lowest level of this protein was observed in control group. No significant associations of IGFs/IGFBPs serum levels with tumor localization, its size and type of affected bone were revealed.

**Conclusions:** IGF-I and IGF-II serum levels in patients with malignant bone tumors are elevated as compared to persons with benign bone lesions and practically healthy people, while serum IGFBP-3 level is the highest in benign bone tumor group. These results allow to suggest that IGF-I and IGF-II could be involved in pathogenesis of bone tumors, and IGFBP-3 might play a protective role in this process.

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## Associations of single nucleotide polymorphisms IGF1.rs7956547, GNRH2.rs3761243 and FGFR3.rs6599400 with bone tumors in Russian population

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**Objectives:** Bone tumors are a rather rare, but difficult in diagnostics and treatment group of oncological diseases. This investigation continues our earlier study of associations of single nucleotide polymorphisms revealed by osteosarcoma group [Mirabello et al., BMC Cancer 11:209, 2011] with bone tumors in Russian population [Naumov et al., Bull Exp Biol Med. 53(6), 2012]. The aim of present study was to detect meaningful changes in genes that are responsible for bone growth and development: insulin-like growth factor 1 (IGF1) gene, growth hormone 1 (GH1) gene, gonadotropin-releasing hormone 2 (GNRH2) gene, fibroblast growth factor 2 (FGF2) gene, fibroblast growth factor receptor 3 (FGFR3) gene, p53 binding protein homolog (MDM2) gene.

**Methods:** 119 patients with various bone neoplasms (osteogenic sarcoma 43, Ewing Sarcoma - 6, chondrosarcoma - 40, malignant fibrous histiocytoma - 2, fibrosarcoma - 1, bone lymphoma - 1, chordoma - 1, giant cell bone tumor 25) undergoing examination and treatment in the department of General Oncology of the Russian N.N. Blokhin Cancer Research Center were included in this study. The control group comprised 93 people without oncological diseases. Genomic DNA was extracted from leukocyte fraction of peripheral blood. The determination of polymorphisms alleles rs7921(GH1), rs7956547(IGF1), rs3761243(GNRH2), rs11737764(FGF2), rs6599400(FGFR3), rs1690916(MDM2) was performed during the reaction of mini-sequencing with following mass-spectrometry measuring of reaction products in time-of-flight mass-spectrometer AutoFlex-III (MALDI-TOF).

**Results:** 3 of 6 polymorphisms showed significant associations with bone neoplasms: IGF1.rs7956547 (risk allele T, OR = 3,28[1,42-7,54], p=0,003), GNRH2.rs3761243 (protective allele C, OR = 0,54[0,3-0,99], p=0,04), FGFR3.rs6599400 (risk allele A, OR = 2,15[1,06-4,34], p=0,03).

**Conclusions:** The studied polymorphisms are located in genes which products are responsible for growth and formation of bone, and they also are involved in tumor progression. It allows to suggest that these polymorphisms might be involved not only in the development of osteosarcoma, but also in the origin of bone tumors as a whole. Our results confirm our recent data on a larger group of patients and detect new significant associations.

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## Diffuse Large B-Cell Lymphoma Presented as Bone Lesions. A study of cases

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**Introduction:** Diffuse large B-cell lymphoma is the most common lymphoma worldwide. Both morphologically and prognostically it represents a diverse spectrum of disease. Primary bone lymphoma is suggested when the patient remains free of extraskkeletal disease for 6 months after diagnosis. Primary B-cell lymphomas has been lately classified as 3 distinct subtypes, which reflect different stages of B-cell differentiation.

**Materials and Methods :** Twenty-eight patients with primary diffuse large B-cell lymphoma of bone were studied. The tumors were subclassified according to the criteria of the WHO standards and evaluated by immunohistochemistry . The spectrum of antigens including bcl-6, CD10, MUM-1, CD 138, bcl-2 (DAKO corporation) helps to investigate the possible relationship of PBDLBCL of bone to stages of normal B-cell differentiation.This review focuses solely on de novo DLBCL presenting with bone involvement without evidence of extraskkeletal disease.

**Results and Conclusions** We report a series of 28 primary bone lymphoma cases with female predominance (10/18), the median age of the patients (48,2), the femur was the most common site of involvement and axial skeleton the second most common location. Most tumors were centroblastic, or centroblastic with multilobated nuclei (20/71%). The majority of tumors (17/62%) were bcl-6 positive, and 15/53% of cases coexpressed CD10. The combination of positive CD10 and bcl-6 markers is currently widely accepted as an immunophenotypic signature for germinal center (GC) –like phenotype. The absence of both markers, 10/37% of cases , were interpreted as indicative of a post germinal center phenotype. The coexpression of MUM-1 and bcl-6, that is exclusive in normal GC B-cells, has been reported in 9/29% of the cases and possibly suggests a late stage of GC differentiation for those MUM1+ cases.

Several clinical studies indicate that patients with primary bone lymphomas have a favorable prognosis. Overall, the outcome in CD10 and bcl-6 positive cases after combined modality therapy was better, than in other groups of the patients. Most tumors showed neither morphologic nor phenotypic evidence for plasmacytic differentiation, suggesting a biologic difference from plasma cell tumors of bone. The expression of CD10 was associated with improved survival.

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## Cytokine spectrum of patients with osteosarcoma

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**Background:** To study the spectrum of patients with osteosarcoma.

**Methods:** 42 patients with histological, verified osteosarcoma were examined, who have been treated at National Cancer Center from 2009 to 2011, male patients predominated – 55.4%, female – 44.6%, correspondingly. Average of patients made up 19.5. For study serum concentration of cytokines was used test – systems of «Vector-Best», Novosibirsk, 2011. Studied cytokine spectrum was presented IL-1 $\beta$ , TNF- $\alpha$ , IL-2, IL-6, IL-10 and VEGF.

**Results:** Serum concentration of IL-1 beta, TFN-alpha and IL-2 in the group of patients with osteosarcoma were increased in 2; 2.4 and 1.5 times correspondingly relative significance of control group. Investigations showed, that serum concentration of IL-1 and IL-6 were increased in 1.3 and 23 times correspondingly, than significance of control group (pConclusion: Thus, obtained data show significant changes in cytokine spectrum of patients' blood with osteosarcoma, which have important significance in forming and progressing of malignant process. Detected disbalance in the contents of main cytokine of immune system in patients with osteosarcoma serves important diagnostic and prognostic criteria in determination further treatment tactics in patients with osteosarcoma.

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## Immunolocalization and Expression of Afadin-6 in Plexiform Neurofibromas

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### Background

Neurofibromatosis type 1 (NF1) is a frequent single-gene disorder that affects the musculoskeletal system and the nervous system. Neurofibromatosis type-1 is inherited in an autosomal dominant manner with an incidence of about 1 in 3000. Tight junctions are specialized cell-cell point of adhesion at the apical region of epithelial and endothelial cells that creates cellular barrier. The Afadin-6 protein is a protein that contains two potential Ras binding domains. The Afadin-6 functionally links the cytoskeleton, through cellular signalling pathways and the cell-cell junctions. This study was carried out to demonstrate the relative expression and cellular localization of Afadin-6 in Plexiform neurofibroma by immunohistochemistry.

### Methods

Informed patient consent was obtained two weeks before surgery and the study has an ethical approval (06/1505/137) of Liverpool Research Ethics Committee. Standard Operating Procedure of the department of Pathology, University of Liverpool was used in the immunohistochemistry technique. Both the test and control tissues were immunostained with Rabbit Anti-AF-6 polyclonal antibody diluted at 1:100-1:200 at (pH 7.0) (Catalogue No. 433280, Invitrogen). Slides were visualised under light microscopy.

### Results

The Afadin-6 immunoreactivity on the perineurial fibroblast cell-cell junction was observed to be weak and localised at the cell-cell junction of the perineurial fibroblast of all the familial. Furthermore, moderate membranous and nuclei immunolocalization of the AF-6 were observed in endothelial and Schwann cells of all the Plexiform Neurofibromas.

### Conclusion

The study suggests that Afadin-6 may be involved in cell proliferation and survival of the neurofibroma cells and therefore becomes a target protein in the management of plexiform neurofibroma which has the potential of transforming to Malignant Peripheral Nerve Sheath Tumour.

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**Extra-axial Chordoma of bone and soft tissues: report of two case.***Antonina Parafioriti<sup>1</sup>, Elisabetta Armiraglio<sup>2</sup>, Andrea Di Bernardo<sup>2</sup>, Primo Andrea Daolio<sup>3</sup>, Roberto Zorzi<sup>3</sup>, Anna Concetta Berardi<sup>2</sup>**<sup>1)</sup> Orthopaedic Institute Gaetano Pini <sup>2)</sup> Pathology Dept, Orthop.Institute G. Pini <sup>3)</sup> Orthopaedic Surgery, Orthop.Inst.G. Pini, Italy*

Chordoma is a rare low-to-intermediate grade malignant bone tumor usually affecting the axial spine of adult patients that shows a distinctive immunophenotype (cytokeratins, S100 and brachyury).

Very few cases of chordoma-like lesions have been described in extra-axial sites where, despite their rarity, they pose problems of differential diagnosis with primary or metastatic epithelioid tumors of soft tissue and bone, in particular with the mixed tumor/myepithelioma/parachordoma family of tumors.

Here we described two cases of extra-axial soft-tissue chordomas.

The first case was a 39 year old woman with a history of swelling and pain of the right arm that, at radiological examination, showed a juxta-osseous mass of 5 cm involving the humerus shaft and consequently underwent mid-humerus resection. The second case was a 58 year old woman with symptoms of knee joint monoarthritis and synovial hyperplasia at the imaging investigations which underwent diagnostic biopsy of the synovial membrane. On histological evaluation both cases showed an epithelioid morphology with mixo-chondroid pattern and a phenotype consistent with chordoma, in particular cytokeratin 19 and brachyury positive reactivity were observed.

The latter is the first case described in intrarticular localization within the synovial membrane to the best of our knowledge. Remarkably both cases were characterized by co-expression of CK 19 and brachyury which is considered highly specific of classic chordoma.

The diagnosis of extra-axial chordoma can be challenging, especially in biopsy specimen, because of the rarity of this entity and the immunomorphological features largely overlapping with other tumors (i.e. epithelioid features, Cytokeratins, S100). However, the recognition of extra-axial chordoma is important given its prognostic and therapeutic implications which are different from those of the other entities that could be mistaken for it.

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## Immunohistochemical evaluation of prognostic markers in giant cell tumors of bone: Tenascin and Periostin as predictor of recurrence and metastasis.

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### AIMS:

Giant cell tumours (GCTs) of bone are lytic neoplasm with variable biological aggressiveness and high recurrence rate that occur mainly in the epiphysis of long bones of young adults. These neoplasms can occasionally metastasize to the lung, but malignant transformation into sarcoma is rare. According to the current state of knowledge, histological features are not considered a valid predictor of recurrence and/or metastasis risk. The aim of this study is to investigate the expression of different markers in classic primary GCT, including some components of the extracellular matrix, P63 and P53 that may help to differentiate patients with increased risk of local recurrence and/or distant metastasis.

### METHODS AND RESULTS:

40 cases of GCT were selected and immunohistochemical analysis of the expression of P63, P53, Tenascin C (TNC) and Periostin (Pn) was performed. A correlation was found between different expression patterns and clinical outcome identifying Tenascin C (TNC) and Pn as the most promising prognostic biological markers.

TNC and Pn immunoreactivity evaluation may complete and integrate the morphologic data, that alone are insufficient to risk-stratify patients, and may lead to a more accurate classification and identification of subgroups with different outcome.

### CONCLUSIONS:

Our study provides encouraging results in the search for potential biomarkers with relevant clinical impact in GCT, suggesting the possible prognostic value of TNC and Pn expression in the identification of those GCT patients with a higher risk of relapse which, consequently, require a closer follow-up and, possibly, an adjuvant medical therapy.

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## Reactive Bone Lesions in Postchemotherapy Pediatric Bone Tumor Specimens: Implications on Surgical Planning by Preoperative MRI

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**Background:** Therapy-associated changes in bone tumor specimens include changes in tumour volume and reactive changes associated with tumor necrosis as well as marrow changes and periosteal reaction.

**Aim:** This study analyzed the accuracy of pre-operative MRI images in determining the local tumor extent before surgery in patients with high-grade osteosarcoma and Ewings sarcoma after neo-adjuvant chemotherapy.

**Methods:** From January 2009 till January 2011, a total number of 75 pediatric patients presented at the Children Cancer Hospital Egypt with malignant tumors in long bones; High-grade osteosarcoma (n=56) and Ewing sarcoma (n=19) patients treated with neo-adjuvant chemotherapy and definitive surgery were analyzed. We compared the accuracy of the intra-osseous extent of the tumor as measured by pre-operative MRI, with the actual extent of the tumor as assessed by gross and microscopic examination of the resected specimens. Difference in measurements of more than 1 cm was considered as discrepancy.

**Results.** The extent of intra-osseous tumor was defined accurately by preoperative MRI in 50 (89%) osteosarcoma cases and 15 Ewings sarcoma cases (78%). The mean overestimation between definitive histopathology and MRI measurements in Osteosarcomas was 3.2 (median = 2.5). In Ewings sarcoma, the mean overestimation by MRI was 2 cm (median = 2.5). In osteosarcoma, the correlation coefficient between maximum radiological dimension determined by pre-operative MRI and by pathology was 0.967 (p-value < 0.001). In Ewing's sarcoma, the correlation coefficient between maximum radiological dimension and pathology was 0.973 (p-value < 0.001). Important causes for inaccurate measurements from MRI included bone marrow changes as edema or focal necrosis, and false positive epiphyseal infiltration.

**Conclusions.** Preoperative evaluation of tumor extent using MRI is a reliable method to assess the local extent of bone tumors in children. These findings are useful in planning surgical limb salvage procedures and stress the ineffectiveness of the "therapy-associated changes" in bone specimens on preoperative radiological estimation of tumor extent. Intra-operative frozen section examination of the margins should be considered as part of the assessment in limb-sparing procedures. More consideration should be given to distinguishing treatment-related reactive changes.

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## Correlation of proliferation index Ki67 with grade and time to recurrence of soft tissue sarcoma

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**Background:** Analysis of correlation of proliferation index Ki67 with grade and time to recurrence of soft tissue sarcomas.

**Methods:** We reviewed 34 patients treated in RCRC RAMS. 53% patients were female, 47% - male. Adult patients - 97%, children - 3%. Soft tissue tumors localized on lower extremities in 47% cases (hip, shank), on upper extremities in 20% cases (shoulder, forearm, hand), on trunk in 24% cases, on head and neck in 9% patients. Histological subtypes were monophasic synovial sarcoma - 32%, malignant fibrous histiocytoma - 23%, liposarcoma - 18%, malignant schwannoma - 6%, and other types in isolated instances. Synovial sarcoma more often observed in young and middle age women, malignant fibrous histiocytoma - in old men, liposarcoma - equally often in middle and old men and women. We observed soft tissue sarcoma grade 2 (FNCLCC) more frequently.

**Results:** Local recurrence development in 35% cases, number of recurrences was from 1 to 6. Distant metastases were in 8 patients (in lungs, bones). We used monoclonal antibody Ki67 (clone MIB-1). Proliferation index Ki67 evaluated in the following way: low level - less than 25% of tumor cells, middle level - 25-50%, high level - more than 50% of tumor cells.

**Conclusion:** Proliferation activity Ki67 increase in cases with high grade soft tissue sarcoma (in grade 1 tumors - low and middle proliferation activity, in grade 2 tumors - middle and high proliferation activity, in grade 3 tumors - only high proliferation activity). Proliferation activity Ki67 increase in recurrent tumors (2-3 times more in comparison with primary tumors). In cases with low level of proliferation index Ki67 were observed long interval to local recurrence and distant metastases. If level of Ki67 was high, time interval to local recurrence was short, lethal outcome occurred often.

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## The significance of the minimal residual disease detection in Ewing sarcoma and primitive neuroectodermal tumor

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**Background:** The Ewing sarcoma and primitive neuroectodermal tumor are bone and soft tissue malignant tumors which occur mainly in children and young adults. A reciprocal translocation resulting in fusion of the EWS gene with a member of the ETS family of transcription factors is highly specific marker for this group of tumors.

**Method:** During the 5 year period, from 2004 to 2008, we have analysed 24 patients, tumor tissue, peripheral blood and bone marrow for the EWS FLI 1 type 1 and type 2. The samples were analyzed with reverse transcriptase polymerase chain reaction method (RT-PCR)

**Results:** 24 tumor samples were analysed at the time of diagnosis. 19 (79,2%) were positive for type 1, 2 (8,3%) were positive for type 2 and 3 (12,5%) were negative. At the same time, 4 (16,6%) blood samples were positive for type 1, 1 (4,2%) was positive for type 2, and 16 (66,7%) were negative for EWS-FLI1 translocation. During the intensive chemotherapy treatment (Vincristine, Doxorubicin, ifosfamide, Etoposide), all the blood and bone marrow specimens were negative. During the follow-up 2(8,3%) patients had positive type 1, 1(4,2%) had positive type 2, 16 (66,7%) had negative blood samples, and due the technical error 5(20,8%) specimens were excluded. In the bone marrow, type 1 were positive in 2 samples, and type 2 in 2 samples. Overall distribution of the bone marrow samples was: 5(20,8%) type 1, 2 (8,3%) type 2.

**Conclusions:** EWS-FLI1 type 1, isolated from tumor tissue, showed to be prognostic factor for better outcome. The bone marrow positive translocation was more valuable prognostic marker than one in the peripheral blood. During our follow-up, all patients who had positive EWS-FLI1 fusion in the bone marrow had been detected with clinical progression or recurrence in the period of 2 to 11 months. Some patients with positive EWS-FLI1 in the blood, after follow-up of even several years hadn't got the recurrence of the disease. EWS-FLI1 positive fusion in the peripheral blood therefore couldn't be reliable prognostic factor for the clinical outcome, and positive bone marrow would definitely be the strong predictive factor for the recurrence or disease progression.

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## Centrosome amplification in primary sarcoma cultures and its association with malignant behavior in tumor

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**Background** - Recent studies have reported that centrosome amplification occurs in various types of malignant and borderline malignant sarcomas. In these tumours, aneuploid karyotypes are strongly associated with centrosome alterations. New evidence on centrosome clustering mechanisms has provided insights on how cancer cells survive with supernumerary centrosomes. We investigated the frequencies of centrosome clustering in primary sarcomas in association with clinical aspects.

**Objective** – The aim of the present study was to standardize the method for isolation and cultivation of tumor cells from samples of sarcoma tissue biopsies for centrosome analysis. and to compare findings in centrosome amplification frequency between different sarcoma subtypes.

**Methods** – 12 samples of sarcomas were collected from 11 patients of the Orthopedics Department at the Barretos Cancer Hospital, Barretos-SP-Brazil between January and September 2012. Primary tumor specimens were finely minced, trypsin treated and cultured in DMEM supplemented with 10% fetal bovine serum and 1% antibiotics. Cells were cultured on coverslips for 3 to 4 days, washed with phosphate-buffered saline (PBS), fixed with 4% paraformaldehyde, and then permeabilized with Triton-X100. The UltraVision Plus detection system was used for centrosome immunostaining and analysis. The cells were incubated overnight with mouse monoclonal anti- $\gamma$ -tubulin following blockade with Ultra-V-Block. After DAB exposure, the slides were subsequently stained with hematoxylin.

Centrosome signals were evaluated in 100 cells to determine centrosome number frequencies.

**Results** – Tumors cell centrosomes were present in variable numbers, located in clusters and/or in isolated points within the nucleus. Quantitative analysis demonstrated differences in centrosome amplification frequency between the different subtypes of sarcomas. Grade I chondrosarcomas presented centrosome amplification in 48% of cells, where as Grade III or recurrent tumors presented 76% of cells with amplification and demonstrated a of 3.5-fold increase in the frequency of cluster formation. For pleomorphic, synovial and myxoid sarcoma the frequencies of clusters was the highest, ranging from 26 to 58.

**Conclusion** – These data related to centrosome amplification were relevant and could contribute to the understanding of the pathological diagnosis and prognosis of bone and soft tissue sarcomas.

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## The expression of Tissue Factor mRNA in bone and soft tissue sarcoma patients

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### Background:

Many tumor cells elicit procoagulant activity by transmembrane tissue factor (TF) leading to the generation of factor Xa, thrombin and fibrin. TF-FactorVIIa complex, FactorXa, and thrombin can promote tumor cell invasion, adhesion, proliferation and cytokine, MMPs and VEGF production. It is reported that TF expressed by tumors is demonstrated to be an independent prognostic indicator for overall survival (OS) in carcinoma. As shown above, there are considerable evidences that coagulation factors play a critical role in tumor malignancy. However, there is no report about correlation between TF and bone sarcoma (BS) and soft tissue sarcoma (STS). The purpose of this study is to elucidate the correlation between TF mRNA expression level and clinicopathological parameters and to predict the prognosis of BS and STS patients.

### Methods:

This study was performed on tumor tissue samples with histologically verified BS (30 patients) and STS (68 patients). The median age of patients was 47.2 years (range 2-85 years). The median follow-up time of patients was 81 months (range 8-159 months). cDNA were synthesized and TF mRNA expression levels was quantified using an endogenous gene (GAPDH). The relation of TF expression levels with clinicopathological parameters and OS was evaluated.

### Results:

TF expression level was enhanced in high grade group than low grade group. TF expression level was higher in the metastatic patients than no-metastatic patients in histological high grade group of STS. In Kaplan Meier analysis, OS were worse for patients with high TF expression group compared with low TF expression group in histological high grade group of STS. However, TF expression level and OS of BS came out of the opposite of STS. These data cannot show statistical significant differences.

### Conclusion:

In this study, we reported that high TF expression is thought to be associated with tumor malignancy in STS. This may have a possibility that the measurement of TF expression contribute to not only prediction of tumor malignancy of STS. These need further study.

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## Features of central venous catheterization in patients with Askin tumor

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**Background:** Treatment of Askin tumor in children - PNET thoraco-pulmonary zone - in the first stage involves holding at least five cycles of chemotherapy requiring the central vein catheterization in the first hours after the diagnosis. In this case, the anatomy of the chest is often changed because of the prevalence of tumor, making the subclavian vein puncture even more dangerous. Implanted venous port is often not possible due to contraindications for general anesthesia. The optimal choice - catheterization of the internal jugular vein on the affected side, it is easier and safer to the femoral vein catheterization.

**Materials and Methods:** From 2010 to 2012, we observed 15 patients with Askin tumor at the age of 6 to 17 years. In 7 (46.6%) of these tumor-induced processes that use mediastinal shift, sprouting dome diaphragm, pushed aside and squeezed the subclavian artery and vein. These patients were performed catheterization of the internal jugular vein on the affected side after the preliminary layout with ultrasound. As a solution to close the catheters between their uses, we use a product containing tauolidine, prevents the formation of biofilm on the inner surface of the catheter. After the 2 courses of chemotherapy (including combinations of Doxorubicin, Vincristine, Cyclophosphamide and Etoposide with

Ifosfamide) the significant regression process and the stabilization of the state were achieved providing these patients with long-term vascular access.

**Results:** no cases of hemo-pneumothorax, trauma adjacent common carotid artery and other anatomical structures, catheter-related infections were observed. In 3 (20%) patients developed catheter thrombosis, which was successfully resolved by adding to it 3 ml of urokinase with exposure of 15 minutes.

**Conclusion:** the internal jugular vein catheterization in patients with contraindications to implantation of subcutaneous venous ports and a high risk of complications when trying to subclavian vein allows to initiate neoadjuvant chemotherapy in minor time. With virtually no risk of complications that can delay the performance of significant treatment. The use of tauolidine between using a catheter allows to avoid infection. However, the presence of an external central venous catheter requires permanent location of children in hospital.

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## Common gene variants in RAD51, XRCC2 and XPD are not associated with clinical outcome in soft-tissue sarcoma patients

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**Background:** DNA repair mechanisms play a major role in cancer risk and progression. Germline variants in DNA repair genes may result in altered gene function and/or activity, thereby causing interindividual differences in a patient's tumor recurrence capacity. In genes of the DNA repair pathway the gene variants RAD51 rs1801320 G>C, XRCC2 rs3218536 G>A and XPD rs13181 A>C have been previously related to genetic predisposition and prognosis of various cancer entities. Therefore, we investigated the association between RAD51 rs1801320 G>C, XRCC2 rs3218536 G>A and XPD rs13181 A>C polymorphisms and time to tumor recurrence (TTR) and overall survival (OS) in soft-tissue sarcoma (STS) patients after curative surgery.

**Methods:** A total of 260 patients were included in this retrospective study. Germline DNA was genotyped by 5'-exonuclease (TaqMan) technology. Genotypes of each polymorphism were tested for association with TTR and OS using univariate and multivariate Cox-regression analysis.

**Results:** A statistically significant association was observed between tumor grade and adjuvant radiotherapy and TTR and between tumor grade and OS. However, no association was found between RAD51 rs1801320 G>C, XRCC2 rs3218536 G>A and XPD rs13181 A>C and TTR and OS in univariate and multivariate analysis including tumor grade and adjuvant radiotherapy.

**Conclusion:** In conclusion, our results underline a prognostic effect of tumor grade and adjuvant radiotherapy in STS patients but indicate no association between RAD51 rs1801320 G>C, XRCC2 rs3218536 G>A and XPD rs13181 A>C and clinical outcome in STS patients after curative surgery.

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## Activation of peroxisome proliferator-activated receptor gamma is a novel therapeutic means for giant cell tumor

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### Introduction:

Peroxisome proliferator-activated receptor gamma (PPAR $\gamma$ ) is a ligand-activated transcription factor that belongs to the nuclear hormone receptor superfamily. PPAR $\gamma$  plays a central role in the differentiation of adipocytes from precursor cells and is reported to exhibit anti-tumorigenic effects on a certain malignancy. Giant cell tumor of bone (GCTB) is a common primary benign tumor, but in some cases behaves aggressively, resulting in tumor recurrence. It is known that stromal cells of GCTB has a key role in the pathogenesis of the tumor rather than the multinucleated giant cell. However, effective therapies against GCTB have not been established to target the stromal cells. Moreover, the therapeutic effects of PPAR $\gamma$  activation on GCTB have not been fully clarified.

### Methods:

We established primary cell lines of GCTB stromal tumor cells from fresh GCTB specimens surgically resected from two patients. These cell lines were treated with zaltoprofen, a nonsteroidal anti-inflammatory drug possessing an ability of activation of PPAR $\gamma$ , or troglitazone, a high-affinity agonist for PPAR $\gamma$ , at different concentrations and then subjected to WST-1 cell proliferation and TUNEL assays. The expression of PPAR $\gamma$  was assessed by immunofluorescent cytochemistry. The adipocytic differentiation of tumor cells was also examined using LipidTOX green neutral-lipid staining.

### Results:

The treatment of 100  $\mu$ M or 200  $\mu$ M zaltoprofen significantly inhibited a cell proliferation of GCTB cells in a dose-dependent manner ( $p < 0.001$ ). The apoptotic indices in TUNEL labeling were approximately 0% in control, 21.9% in 100  $\mu$ M ( $p < 0.001$ ) and 48.1% in 200  $\mu$ M ( $p < 0.001$ ) of zaltoprofen treatment. The labeling indices of PPAR $\gamma$ -positive cells were significantly higher than those in control after 24 hour of zaltoprofen treatment. Troglitazone treatment also demonstrated an inhibition of the cellular proliferation. Moreover, zaltoprofen treatment significantly increased labeling indices of LipidTOX Green neutral-lipid staining.

### Conclusions:

These findings demonstrated that zaltoprofen could induce anti-tumor effects on GCTB cells, and also promoted the differentiation into an adipocytic lineage in remained tumor cells via an activation of PPAR $\gamma$ . This is the first study, to our knowledge, that activation of PPAR $\gamma$  could be a novel therapeutic tool against GCTB.

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## Epidemiological data of patients presenting to a Tertiary Cancer Centre

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**Introduction:** The study was conducted to know the frequency and spectrum of number of bone and soft tissue (BST) tumours presenting to our institute and analyze the incidence and stage of these at presentation.

**Material and methods:** This prospective observational study included all new patients seen in BST-Disease Management Group (DMG) from 01/01/2010 to 31/12/2010. An audit form was devised to capture all the relevant information.

**Results:** Out of total 31951 new patients registered at our institute, 1627 (5%) were registered primarily in the BST-DMG and 380 patients were referred from other services. Of a total 2007 patients, 60% (n=1203) were bone tumors, 36 % (n=723) were soft tissue tumors. Details of primary site of affection were not known in 4% (n=81) patients. In bone tumors, 66% were malignant, 15% were benign and 19% were lesions of non-neoplastic etiology. Amongst malignant tumors, osteosarcoma (43%) was commonest followed by PNET/Ewing's (27%) and chondrosarcoma (11%). Giant cell tumor was the most common benign bone tumor. Of soft tissue lesions 81% (n=587) were malignant of which 75% (n=413) were of mesenchymal origin and 25% (n=138) were of cutaneous origin. Synovial sarcoma (22.5%) was most common mesenchymal tumor. 29% of bone tumors and 32 % of soft tissue tumors had metastasized at presentation.

**Conclusion:** The study has a limitation of being a hospital based census and thus may not give the exact reflection of incidence in general population. This study will help assess the gap between the number of patients and infrastructure available and guide us optimally utilize resources to provide best possible care. It can help the institute frame and implement disease specific protocols. Continued data collection and follow up can provide valuable information on long term survival, treatment related toxicities and incidence of second malignancies. This data can be extrapolated to national level to identify the need of infrastructure and human resources.

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## Returning to life after treatment end: quality of life in survivors of osteosarcoma of developmental age

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### Background

Tumors in developmental age can bring psychological development and quality of life issues. Typically osteosarcoma affects mainly adolescents at a critical stage of their mental and physical growth. When treatment ends, eventual psychosocial problems related to the experience of illness and its sequelae may remain undetected. Clinical experience suggests that some surviving patients missing important evolutive stages (i.e. relationships, working identity, planning future). Others, on the contrary, can achieve adequate adaptation level and even demonstrate a greater strength than healthy peers in proposing high goals. The factors predicting the variability of outcome are still unclear. The personality, that defines the psychological and behavioral variability between people, is stable throughout life and can be a useful indicator of long-term functioning.

This study aims to assess the quality of life and the personality features in surviving patients treated for childhood osteosarcoma.

### Methods

The study enrolled patients treated at the pediatric oncology unit of the Fondazione IRCCS National Cancer Institute and Pini Hospital in Milan. Patients were at least eighteen years old and had completed treatment at least from five years. Data collection begun in September 2011. The following self-report questionnaires were delivered during the follow-up visits or sent by mail: TESS, SF-36, QOL-CS, Big Five Questionnaire, SCL-90.

### Results

Until now, 19 questionnaires were completed. Results highlight that quality of life is general adequate, but 5 (26%) of these guys have dropped out of school or do not yet have a job, 3 patients were followed over the years in a course of psychotherapy and a girl, after the completion of the questionnaire, asked us psychological support.

### Conclusion

The long-term adjustment of cancer survivors is an important area of clinical intervention. Preliminary results suggest that in some cases a normal life return can be complicated. Quality of life should be evaluated during follow-up to identify situations may need a support/intervention.

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## **Bone Giant Cell Tumor: p53 and ki-67 expression correlation between the presence of lung metastasis and biological behavior.**

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Retrospectively, the authors have the objective to show the results on the correlation between the p53 and ki-67 expression and the presence of lung metastasis and the biological behavior of the giant cell tumors. The expression graduation was made by immunohistochemical study. As a secondary objective, to find an epidemiological face of the giant cell tumors, from 2003 to 2006 at the authors hospital.

From 46 patients, 21(45.65%) were female and 25(54.35%) were male, age variety from 13 to 75 years (average 33.9 years) and average follow up was 22 months.

The results show that p53 was negative in 54.5% cases, and had poor expression(+/++++) in 31.08% cases. Ki-67 was positive in 68.02% cases.

The authors conclude that the giant cell tumors have a high range of cellular proliferation and had bad expression on the prognostic marker

Key words

Giant cell tumors, tumor markers, lung metastasis

Introduction

The Giant Cell Tumor(GCT) is is considered a aggressive benign bone tumor, with a inert biological behavior. Histological is typically seen with fusiforms cells and by the presence of numerous giant cells multinucleated(gigantócitos), around the connective stroma(?) in the tumor.

Radiografically, the GCT in it's classic shown, as a epiphisis lesion, litic, insuflativa, excentric, sometimes breaking the bone cortical

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## Non-diagnostic biopsies in an oncology unit. Incidence and consequences.

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### Background:

Obtaining an accurate diagnosis is the aim of any biopsy of a musculo-skeletal lesion. This study investigated the accuracy of biopsies carried out at our unit over a three month period and also identified the consequences of a non-diagnostic biopsies.

**Method:** All patients undergoing a biopsy were identified from our MDT records over a three month period. The biopsy diagnosis was correlated with the eventual diagnosis and in those in whom there was a discrepancy the effects of the initial non-diagnostic biopsy was investigated.

**Results:** 222 patients had a biopsy over a three month period, 94 Jamshidi bone biopsies, 59 Trucut biopsies, 28 image guided (CT or U/S) and 41 open biopsies. There were 27 non-diagnostic biopsies but in 16 cases the MDT agreed a diagnosis and management and no further biopsy was required. There were thus 11 non-diagnostic biopsies (5%) and on average these led to a delay in reaching a diagnosis of 3 weeks which was usually reached through one or more further biopsies, mostly image guided. The non-diagnostic rate was highest for needle biopsies (5%) and open biopsies (5%). In terms of eventual diagnosis the initial failure rate was lowest for malignant bone and soft tissue sarcomas (3 of 50, 6%) and highest for lymphomas (15%) and for non-oncological lesions eg haemangiomas. Of the patients with non-diagnostic biopsies, there was the anxiety of waiting for a confirmed diagnosis (and 7 of the 11 turned out to have a malignancy). One patient still does not have a definite diagnosis. In no case was there any significant difference in treatment as a result of a non-diagnostic biopsy.

### Conclusion:

Patients need to be warned that whatever method of biopsy is used there will be a possible failure to obtain a diagnosis. Whilst a non-diagnostic biopsy may rule out malignancy and be accepted by the MDT, repeat biopsy is required in 60% of those cases. In no case was a patients management or outcome significantly altered by a non-diagnostic initial biopsy in this cohort.

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## Ultrasonography in the diagnosis of tumours of the hand

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**Introduction:** One of the basic methods for diagnosing pathological processes that occur in the hand is ultrasonography.

**Materials and Methods:** The study carried out using the ultrasound system LOGIQ-3 PRO supplied with an ultrasound scanner of high quality class and multipower sensor 8L (period between 2001 and 2012). Longitudinal and transverse scanning was performed before surgery, after wound healing and at long-term follow-ups. Tumours were detected, their size, structure and contours were estimated, and topical diagnosis was performed. The study was conducted in 143 patients with tumours of the hand.

**Results:** In cases of tumour-like diseases of hand tendons, a discontinuity of their contours can be detected with appearing hyperechogenic defect zone. In a number of cases, lesions to nerve trunks and their shift due to a tumour can be clearly identified. If the joint is involved, the changes in width and uniformity of the joint space, lytic alterations of the articular surfaces are revealed. In cases of malignant tumours of hand bones (chondrosarcoma), thickening of the cortical layer round the tumour, usuration and collapse (fibrosarcoma and osteosarcoma) of the latter can be noted. In peripheral types, there is destruction focus, bone lysis and the exit into soft tissues. Diagnostic ultrasound enables observation of the repair process in the postoperative rehabilitation period, in particular after suturing tendons and nerves, and osteoplasty (organ salvage surgeries).

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## Ultrasound-guided biopsy in bone lesions: how and when it can be done. Preliminary results.

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### BACKGROUND

Bone biopsy is usually under CT guidance. Compared to US guided biopsy, this technique is extremely precise but it takes more time in execution and in some geographic areas is less available. The aim of this study is to propose US guided biopsy in specified bone lesions with cortex interruption but without soft tissue involvement.

### METHODS

From January to December 2012, eleven patients (7 males, average age 57 years old, range 28-81) underwent an US guided biopsy for a bone lesion. The lesions, always characterized by a cortex interruption, were located in the lower limb (3 cases), in the upper limb (4), in the chest (3), and in the pelvis (1). MyLab Twice sonography (Esaote, Genova, Italy) with multifrequency probes and sterilizable biopsy kit was used. In 9 patients only a tru-cut needle had been used, whilst in 2 cases was necessary to take same samples also with a trephine bone needle. To assess the diagnostic accuracy we evaluated agreement between the diagnosis made on bone tissue specimens from needle biopsy and either the final diagnosis or the clinical evolution (whether not further surgically treated) by means of Cohen's kappa. This coefficient is a statistical measure of inter-rater agreement for qualitative (categorical) items.

### RESULTS

In 9 cases out of 11 the diagnosis was obtained correctly. The diagnosis were myeloma (3 cases), metastases of carcinoma (2), metastases of sarcoma (1), giant cell of the bone (2), Tietze's disease (1), not diagnostic biopsy (2). On 11 patients 5 tumors types were diagnosed, so that 5 items were considered for Kappa coefficient calculation. In two patients insufficient material was obtained to allow a histological diagnosis. In the remainder 9 patients a perfect agreement was observed ( $k=1$ ,  $p$ ).

### CONCLUSION

In accurately selected cases the biopsy of bone lesions can be performed under US guide. This technique is eventually more time effective and does not use ionizing radiation. Further studies are needed to confirm our results.

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## Can trauma lead or mislead to the diagnosis of soft tissue sarcomas?

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### Background

Clinical symptoms in soft tissue sarcomas (STS) are quite easy to investigate but often misleading. The main reason of misdiagnosis is the high frequency of benign or not-tumoural diagnosis comparing to malignant lesions. To date still many patients are initially treated for "hematomas" or "cysts" and then referred to a Sarcoma Unit worsening the prognosis. Many patients remind a trauma and consider it as a possible cause of sarcoma developing. The aim of the study is to determine whether a trauma can represent an alert for the diagnosis of a STS.

### Methods

Fifty-one patients (26 males, 61 years old average, range 24-84 years) with a diagnosis of STS have been investigated according to the presence or not of a direct/indirect trauma in the same anatomical site of the STS referring to the previous medical history. Furthermore patients have been asked for the presence or not of a subcutaneous hematoma.

### Results

Eighteen patients remembered a trauma. Nine were direct trauma and 9 indirect (muscle elongation, repetitive microtrauma, physical effort). Hematoma was present only in 4 cases: in 2 cases referred by the patient but not evaluated by a physician after a trauma (1 direct and 1 indirect), in 2 cases without a previous trauma (2 superficial STS with superficial veins involvement). No statistically significant association between trauma and hematoma was demonstrated ( $p > 0,05$ , Fisher exact test)

### Conclusion

Despite clinical symptoms of STS are not specific, only an objectivable subcutaneous hematoma is to be considered an obvious sign of a relevant trauma. Hematoma should not be considered a possible diagnosis if there is no trauma and no "blood-thinning" therapy. On the other side a trauma can often represent an alert to make the patient notice the presence of a lump. The effect of a direct trauma in the developing of a STS is not demonstrated. Further studies can help in favouring the early diagnosis of STS and the correct referral to a Sarcoma Unit.

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## TREATMENT MODALITIES AND FOLLOW UP OF CHILDREN WITH PERIPHERAL NERVE SHEET TUMOR 15 YEARS SINGLE INSTITUTION EXPERIENCE

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**Background :** The objective of the study was to analyze the treatment modalities in cases of malignant peripheral nerve sheath tumor (MPNST) in children treated during a 15 year period in the Pediatric Department of the Institute for Oncology and Radiology, Serbia.

**Methods:** During the period of 1996-2011 there were 9 children (6 male and 3 female) with a median age of 14 years (age range of 4 years to 17 years) treated using a multimodal therapeutic approach that included surgery, chemotherapy and radiotherapy. The patients presented with primary tumor sites as follows: 5 on the extremities, 1 in the sacrum, 2 in the head and neck and one localized in the shoulder. The majority of the patients (8 out of the 9 patients) had large tumors (>5cm). Two of the patients were affected by neurofibromatosis 1.

**Results:** Treatment commenced in 5 patients with a gross total tumor resection and they were classified as IRS group I (histologically free margins found on biopsy). Another 4 patients were classified as IRS group III and surgery was delayed till after a neoadjuvant chemotherapy treatment (of between 3 and 5 cycles). Two patients had amputations and 2 conservative resections with macroscopic residual tumor.

Chemotherapy was administered to all patients, neoadjuvant in 4 of the patients. A response to chemotherapy was seen in 2 patients in the IRS group III and 2 patients experienced a progression of disease.

The chemotherapy regimens used were VACA in 4 patients, CEVAIE in 3 patients, 1 patient was treated according to EE99 protocol and 1 according to EpSSG NRSTS 2005 protocol.

Seven of the patients had radiotherapy concomitantly with the chemotherapy. The total dose ranged from 55 to 60 Gy.

Eight of the patients are now in the follow-up period with no evidence of disease for between 1 and 14 years.

**Conclusion:** Multimodal treatment is effective in children with MPNST. According to our study the time of diagnosis, IRS group, site and absence of metastasis are important predictors of survival.

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## Myositis ossificans: keep the scalpel away!

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**Background:** Myositis ossificans is a rare benign disease. The ectopic bone formation within muscle and soft tissues that characterizes Myositis Ossificans, follows, in most cases, a traumatic event. Differential diagnosis includes osteosarcoma, soft tissue sarcoma and osteomyelitis. The purpose of this study is to characterize a series of patients with Myositis Ossificans, treated in a Pediatric Orthopaedics Department.

**Methods:** Retrospective analysis of all pediatric patients treated in our institution for Myositis ossificans, between 2008 and 2012. Data was collected regarding age, sex, history of trauma, clinical presentation, imaging features, treatment options and follow-up.

**Results:** 7 patients were identified with Myositis Ossificans: 4 males and 3 females, aged between 7 and 15 years. Five patients were referred due to a soft tissue mass and 2 patients had the diagnosis made prior to referral. A previous traumatic event was identified in all cases. The anatomic distribution of the lesions was diverse: 4 in the thigh, 2 in the shoulder and 1 in the calf. Radiologically, all lesions showed a peripheral mature ossification and radiolucent center; 4 lesions were adjacent to cortical bone, with a marked periosteal reaction. Biopsy was needed in one case, to confirm the diagnosis in a patient with worsening pain. Conservative treatment was undertaken in 6 patients, with spontaneous regression of the lesions. One patient had surgical excision of the lesion.

**Conclusion:** All cases in our series had a traumatic etiology. The diagnosis of Myositis Ossificans is based upon clinical presentation and imaging features. In most cases, biopsy is not needed and treatment should be conservative, as spontaneous regression is the rule. Surgical treatment is reserved to persistent painful situations and should be performed after the maturation of the lesion, usually after 6 months.

We present an important case series of Myositis Ossificans in the pediatric population. Care should be taken to avoid unnecessary and harmful interventions in these patients.

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## Elevated preoperative neutrophil/lymphocyte ratio is associated with poor prognosis in soft-tissue sarcoma patients

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**Background:** Recent data indicate that tumour microenvironment, which is influenced by inflammatory cells, plays a crucial role in cancer progression and clinical outcome of patients. In the present study we investigated the prognostic relevance of preoperative neutrophil/lymphocyte (N/L) ratio on time to tumour recurrence (TTR) and overall survival (OS) in soft-tissue sarcoma (STS) patients who underwent curative surgical resection.

**Methods:** 260 STS patients were included in this retrospective study. Kaplan Meier curves and multivariate Cox proportional models were calculated for TTR and OS.

**Results:** In univariate analysis, elevated N/L ratio was significantly associated with decreased TTR (HR, 2.340; 95%CI, 1.286-4.259; p=0.005) and remained significant in the multivariate analysis (HR, 2.183; 95%CI, 1.191-4.003; p=0.012). Patients with elevated N/L ratio showed a median TTR of 78.7 months. In contrast, patients with low N/L ratio had a median TTR of 99.8 months. Regarding OS, elevated N/L ratio was also significantly associated with decreased survival in univariate analysis (HR, 2.896; 95%CI, 1.810-4.634; p=0.001) and remained significant in multivariate analysis (HR, 2.615; 95%CI, 1.616-4.231; p=0.001).

**Conclusion:** In conclusion, our findings suggest that an elevated preoperative N/L ratio predicts poor clinical outcome in STS patients and may serve as a cost-effective and broadly available independent prognostic biomarker.

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## Oncological outcomes of soft tissue sarcomas in the distal extremities

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### Background

Management of soft tissue sarcomas in the distal extremities can be challenging with patients presenting late and a high proportion of lesions inadvertently excised. Few studies have assessed the outcomes of sarcomas in this location. This study looks at the oncological outcomes of patients with soft-tissue sarcomas in the distal extremities managed at a regional tumour centre in the United Kingdom.

### Methods

The centre database was used to identify all patients with distal extremity soft tissue sarcomas between 1985 and 2012. Patient, tumour, treatment and outcome data was collected from the database and medical records.

### Results

800 patients were included in this study. Of 2667 soft tissue sarcomas seen at the unit, 244 (9%) were located below the elbow while 556 (21%) patients had sarcomas below the knee. There were 432 males and 368 females with a mean age of 49.9 years (2 to 92). The three most common diagnoses were synovial sarcoma (18%), myxofibrosarcoma (8%) and clear cell sarcoma (4%). 38% of the sarcomas were superficial while 40% of them had inadvertent excision carried out elsewhere and presented late. Local excision was carried out in 496 patients (74.7%) and amputation in 156 (23.5%).

The overall risk of local recurrence was 13.7% in this series with risk increased by an involved margin, type of tumour or an inadvertent biopsy. The overall survival rate at five years was 58% and was related to the grade, size, type and depth of the tumour and patient age.

### Conclusion

This large series has shown that the oncological outcomes of soft tissue sarcomas of the distal extremities are similar to other sites. It highlights that a clear margin of excision is essential to achieve local control and that inadvertent excision can increase the risk of local recurrence.

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## OSTEOSARCOMA IN PATIENTS WITH ROTHMUND-THOMSON SYNDROME

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**Background:** Rothmund-Thomson syndrome (RTS) is associated with an increased risk of osteosarcoma, but information about affected patients is limited. This retrospective analysis explored the clinical features of high-grade osteosarcomas in patients with RTS and outcome after multimodal therapy.

**Methods:** The Cooperative Osteosarcoma Study Group (COSS) database was searched for eligible patients. Seven patients with high-grade osteosarcoma had a diagnosis of RTS and their patient-, tumor- and treatment-related variables and outcome were reviewed.

**Results:** Median age at diagnosis was 13 years (range 7-16), 5 were female, 2 male. Tumors involved proximal tibia (4), distal tibia (1), distal fibula (1) and proximal ulna (1). Most frequent subtypes were osteoblastic (3) and malignant fibrous-histiocytoma-like osteosarcoma (2). Three patients had metastatic disease at diagnosis. All patients were treated with surgery and chemotherapy according to COSS-protocols. All but one were underweight at start of treatment, at least four needed nutrition as support during therapy. Four patients received chemotherapy as scheduled, the other three required dose modifications and terminated treatment prematurely. A wide resection of the primary tumor was achieved in all individuals. Two of three patients failed to achieve surgical clearance of their primary metastases and died, the third relapsed with multiple metastases and also died. Two of the four patients with localized disease remained alive in 1st complete remission (CR), 10.5 and 17.6 years after diagnosis, a third patient was in 2nd CR after surgery and chemotherapy for recurrence (solitary lung metastasis), with a follow-up of 13.0 years. The fourth patient, for whom osteosarcoma was already the third primary malignancy, died of acute leukemia, 7.0 years after diagnosis and while still in 1st CR of osteosarcoma.

**Conclusion:** Patients with osteosarcoma in RTS may be cured with appropriate multimodal therapy. They should be treated like other osteosarcoma patients but individual features and special support have to be considered.

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## Difficulties of morphological diagnosis of telangiectatic osteosarcomas.

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Has been analyzed the biopsy and surgical material of patients who had been operated in clinic CITO as well as consulting cases with the diagnosis telangiectatic osteosarcoma (TOS) for the last 12 years. The analysis of the data has shown that for the investigated period of time TOS was found in 71 cases. TOS most commonly affects the femur (31%), tibia (26,8%) and humerus (15,5%). Lesions were centered around the knee in 46,5% (n=33) of cases.

Most of the lesions were located in the metaphyseal region, but usually they extended into the epiphysis. The lesions were poorly marginated and usually characterized by essentially pure lytic destruction without any significant sclerosis. There were seen extensive cortical expansion or destruction and often a soft tissue mass.

Conventional TOS is a high-grade lesion with easily recognizable sarcomatous septa. Usually there is a high degree of nuclear atypia, cellular pleomorphism, and numerous atypical mitoses.

These areas, although only focally present, are easily recognized as malignant and can almost always be found. However, well known significant difficulties in the differential diagnosis between low-grade TOS and benign aneurismal bone cyst. Microscopic examination shows similarity of histological structure of low-grade TOS and aneurysmal bone cyst. Areas of stroma look like as benign aneurysmal bone cyst are present. It should be noted that the atypical cells can be determined only on the periphery of the tumor cavity, malignant cells have a high degree of differentiation, the number of tumor osteoid are minimal, there are areas of tissue in which the cellular elements and osteoid have not signs of atypia, osteoclast-like cells located in the edges of the cysts and cavities tumor.

TOS should be distinguished principally from aneurysmal bone cyst. The weak signs of cellular atypia are especially revealed in the study of cytological preparations.

If in biopsies had been detected the TOS-LG, then were performed surgery in the form of extended marginal bone resection, the removal of abnormal tissue, electrocoagulation, alloplastica of defects. Later patients were observed in specialized hospitals.

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## Oncological outcomes of osteosarcomas in the upper distal extremity

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### Background

Osteosarcomas rarely arise in the upper distal extremity. Few studies have assessed the outcomes of osteosarcomas in this location and there are considerable challenges in surgical management. This study looks at the oncological outcomes of patients with osteosarcomas in the upper distal extremity managed at a regional tumour centre in the United Kingdom.

### Methods

The centre database was used to identify all patients with osteosarcomas in the elbow or distally between 1985 to 2012. Patient, tumour, treatment and outcome data was collected from the database and medical records.

### Results

30 patients were included in this study. There were 14 males and 16 females with a mean age of 36.4 years (9 to 90). 18 osteosarcomas were located in the forearm bones (60%), 9 in the elbow (30%) and 3 (10%) in the hand. The two most common sub-diagnoses were parosteal (28%) and osteoblastic osteosarcomas (16%). Local excision was carried out in 15 patients (51.7%), 4 patients underwent endoprosthesis replacement (13.8%) and 9 amputation (31%).

The overall risk of local recurrence was 14.4% in this series with risk increased by older age, grade and type of tumour. The overall survival rate at five years was 67% and was related to the grade, type of the tumour, type of surgery and patient age.

### Conclusion

This series has shown that patients with osteosarcomas of the upper distal extremities have favorable outcomes with current treatment methods. It highlights that tumour characteristics and patient age impact both on local control and overall survival.

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## Clinical outcomes in the oldest old patients (85 years or older) with musculoskeletal sarcomas.

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### Purpose

The number of sarcoma patient diagnosed in the oldest old population supposed to increase due to the increasing life expectancy in Japan. The purpose of this study was to evaluate the clinical outcomes in the oldest old patients (85 years or older) with musculoskeletal sarcomas.

### Patients and Methods

Between 1988 and 2012, 17 patients were treated at our institution. 3 male and 14 female were studied. The mean age at presentation was 89 years (85-97). There were one malignant bone tumors and 16 soft tissue sarcomas. The tumors were histologically diagnosed as follows: 7 malignant fibrous histiocytomas, 4 liposarcomas, 2 extra-skeletal chondrosarcomas, 2 myxofibrosarcomas, one chondrosarcoma and one malignant peripheral nerve sheath tumor. Overall survival (OS) time was taken from the date of diagnosis for the primary tumor to the date when the patients were documented to be alive or the date when the patients passed away. Disease-specific survival (DSS) time was taken from the date of diagnosis for the primary tumor to the date when the patients were documented to be alive or the date when the patients passed away from sarcoma.

### Result

Thirteen of 17 patients underwent surgery for the primary tumors. The remaining 4 patients were treated with radiotherapy for severe comorbidity. At the time of review, 5 patients were alive and disease free. 6 patients died of sarcomas, and 6 patients died of other causes. OS in all patients was 70% at 1 year and 37% at 2 years, respectively. DSS in all patients was 82% at 1 year and 73% at 2 years. Age (85-90 vs. 90-97) and treatment (surgery vs. radiation) were not significantly related to OS and DSS.

### Conclusion

The oldest old sarcoma patients are supposed to increase in the developed nation because of increasing life expectancy. 2-years-OS in the oldest old sarcoma patients was 37%. The poor prognosis was mainly due to the fact that the half of dead patients died of other disease. In the treatment of them, post-operative careful management concerning the patients complication are warrant.

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## Circulating Transforming Growth Factor-Beta1 Levels in Pediatric Bone Sarcoma Patients

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### Background

Transforming growth factor-Beta (TGF-B1) has an important role in wound healing, angiogenesis, immunoregulation and cancer. TGF-beta plays a major role in cancer by suppressing tumor growth in the early phase of neoplasia, while promoting tumor progression and metastasis in later phases. We aimed to identify the clinical significance of circulating levels of TGF-beta1 as a tumor marker in bone sarcomas.

### Methods

Serum TGF-B1 levels were measured by ELISA in sera of 31 patients with osteosarcoma, 14 patients with Ewing sarcoma before and after treatment and 22 healthy controls.

### Results

Pretreatment mean serum TGF-beta 1 levels were 44,8 ng/ml in osteosarcoma, 46,2 ng/ml in ewing sarcoma and 45.4 ng/ml in control groups. Posttreatment mean serum TGF-beta 1 levels were 42,2 ng/ml in osteosarcoma, 41,2 ng/ml in ewing sarcoma group. Serum TGF-beta 1 level in metastatic disease was 48.1 ng/ml, in non metastatik disease 44,5 ng/ml. The differences between groups and pre and post treatment levels were not significant statistically.

### Conclusion

We could not find any diagnostic and prognostic value of TGF beta 1 in pediatric bone sarcomas.

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## Primary malignant bone tumors of the scapula - A retrospective single-center study of 27 consecutive cases

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Primary malignant bone tumors of the scapula are very rare. Apart from limited case reports international literature on flat bone sarcoma is exiguous and not much is known about the oncological outcome.

By database analysis of the Vienna Bone and Soft Tissue Tumor Registry, we retrospectively identified 27 patients diagnosed with a primary malignant bone tumor of the scapula treated between 1954 and 2011. This included 15 males and 12 females with a mean age of 39.1 years (range, 7.5-79.3 years). The most frequent tumors were chondrosarcoma (40%), Ewing's Sarcoma/PNET (19%), Osteosarcoma (11%) and Hemangiopericytoma (7%). The average time of follow-up was 36 months ( $\pm 21$  month).

Eleven patients received chemotherapy and 12 had radiotherapy. Wide resection was performed in 18 patients (67%). In five patients (19%) no further resection of the tumor was performed after biopsy due to multiple metastasis or inoperability. Postoperative complications comprised two nerve lesions, one seroma, one wound necrosis, and one thrombosis of the arm. Five patients (19%) were diagnosed with metastasis after a mean time of 8 months post surgery, while two patients (7%) suffered local recurrence at an average of 8 months post surgery. The overall patient survival was 58% at one year and 24% at five years. The corresponding median survival was 17 months.

The overall prognosis of primary malignant bone tumors of the scapula remains to be inferior compared to extremity sarcoma. Large-scale studies on these rare entities will be required to identify successful adjuvant treatment regimens.

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## Axial osteosarcoma: a 25 year monoinstitutional experience in patients younger than 19 years.

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**Background.** The survival of patients with pelvic or axial osteosarcoma (OS) remains poor and the management of these patients is particularly challenging.

**Patients and methods.** Object of this study is a cohort of unselected patients aged Results. Twenty patients between 3-19 years (median age 14) were included. Five patients were metastatic. The most frequent histological subtype was chondroblastic OS (45%) followed by osteoblastic OS (30%). Eight patients had pelvic OS, 8 axial OS and 4 mandible/maxilla OS. All patients received chemotherapy. Necrosis post chemotherapy was evaluable in 9 patients ( $\geq 90\%$  in 3 cases). Surgery was performed in 12 patients (3 amputations). Radiotherapy was delivered in 7 patients (total dose 24-60 Gy). Median follow-up was 35 months (8-276), 5-year overall survival was 40% and 5-year event free survival was 37%.

Six patients are alive: 2 with pelvic OS (both had a good response to chemotherapy, one underwent hemipelvectomy and the other received radiotherapy); 1 with axial and multicentric OS (good histological response and radical surgery); 3 with mandible/maxilla OS (a fourth patient died of sepsis during chemotherapy). One patient with axial OS died because of a second bone tumor and another one for breast cancer. We highlight that 6 patients had a p53 mutation: 2 are alive, 2 died for OS, 1 for breast cancer, 1 for glioblastoma.

**Conclusion.** Adequate local treatment and good pathological response are relevant for prognosis of axial OS, that remains dismal. An impressive number of p53 mutations are reported in our series.

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## Risk of amputation after unplanned excision

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**Background:** Unplanned excisions of soft tissue sarcoma may adversely affect local recurrence and overall survival. Tumor bed excisions are recommended after most cases of unplanned excision, although these procedures may be more extensive compared to planned excisions and skin grafting, muscle flaps or even amputation are applied for those patients. We compared patients who had tumor bed excision after unplanned excisions to those who had initial procedures in our institution. The type of surgical procedure was assessed. We expected a higher incidence of amputation and flap/skin grafts for those who had unplanned excisions.

**Methods:** Patients diagnosed with soft tissue sarcomas and who underwent surgical excision of tumor at the Cancer Institute Hospital in Tokyo between 1978 to 2009 were retrospectively reviewed. Age, histologic diagnosis, grade, tumor location, size, adjuvant treatments, surgical procedure (amputation, limb-sparing procedure) and flap or skin graft procedures were reviewed for each patient. We excised the tumor bed with 2cm of margins for high grade tumors and 1cm margins for low grade tumors. Muscle fascia was considered as a barrier when we excised a tumor. We used radiation only when a positive margin was detected after tumor bed excision. All variables were analyzed with Chi square test.

**Results:** 917 patients with a median age at diagnosis of 52-years were eligible for analysis. 76 % of patients had initial surgical excision in our hospital and 24 % of patients had tumor bed excision after unplanned excision elsewhere. Those who had unplanned excisions did not have an increased risk of having an amputation, but were more likely to require additional soft tissue coverage with muscle flaps or skin grafting ( $p < 0.001$ ).

**Conclusions:** Unplanned excisions did not increase the risk of amputation probably because patients with larger tumors are more likely to be referred to cancer centers before intervention than smaller ones. Wounds following unplanned excisions were more likely to require additional soft tissue coverage with muscle flap or skin grafting than were those done as an initial tumor resection.

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## Chondrosarcoma: Does a pathological fracture of the femur have prognostic importance?

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**Background:** The incidence and implication of a pathological fracture in patients with chondrosarcoma of the femur is not clear. The aim of this study is to report overall survival, local recurrence and development of metastasis in a group of patients with chondrosarcoma that suffered a pathological fracture of their femur.

**Methods:** We performed a retrospective review of 182 patients with chondrosarcoma of the femur treated by oncologic surgery. Mean age at diagnosis was 50.5 year old (range 8-90) and mean follow-up was 110 months (range: 3-216). Patients were divided into two groups whether they presented with or without a pathological fracture of the femur. Cancer specific overall survival, development of metastasis, and local recurrence were analyzed. A subgroup comparative analysis of both groups by histologic grade was done.

**Results:** Thirty-nine patients suffered a pathological fracture of the femur. Seventy-two percent of these fractures occurred in the proximal femur and 79% were grade 2, 3 or dedifferentiated tumors. The local recurrence rate of pathological fracture group was 33% and 24% for control group ( $p=0.14$ ). For grade 3 and dedifferentiated, a pathological fracture significantly increased the risk of local recurrence ( $p=0.002$ ). Pathological fracture group developed metastasis in 59% of the patients versus 27% for control group ( $p=0.0003$ ). Five and ten year overall survival in the fracture group were 52% and 35%, lower than in the control group (77% and 67%) ( $p=0.0004$ ). Subgroup analysis by histologic grade revealed that a pathologic fracture in grade 1 & 2 tumours was significantly associated with lower survival (84% vs 73% 5year survival,  $p=0.03$ ) while it only approached significance for grade 3 & de-differentiated tumours (35% vs 10% 5year survival,  $p=0.09$ ).

**Conclusion:** A pathological fracture of the femur has a negative prognostic influence in patients with chondrosarcoma.

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## Transosseous osteosynthesis in the complex treatment tumours of the hand bones

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**Introduction:** Limb salvage treatment of the patients with oncological pathology is considered to be difficult due to the necessity to restore not only anatomical integrity but also hand function.

**Materials and Methods:** The material for the analysis were 204 medical records of the patients who underwent treatment between 1992 and 2012 in the center of hand surgery with application of the apparatuses of external fixation for hand bones tumours. Primary reconstruction procedures considerably reduce the treatment period. The fixator for transosseous osteosynthesis was applied after bone resection due to tumour. That aimed preservation of the operated ray anatomical length. In cases of small bone defects the grafts were placed into the defect area followed by mild compression in the fixator to accelerate the reparative process. In extensive defects, graft was mandatory fixed through additional wires to the fixator. Application of the apparatuses enables stable fixation and the possibility to train motion to restore the functioning of tendons and joints.

**Results:** Long-term follow-ups were studied in 174 patients in the period from 1 to 20 years. Tumour recurrence observed in 22 cases (15 of them were malignant tumours). All these patients were reoperated after thorough examination.

**Conclusion:** The use of external fixators in the treatment of short tubular bones tumours of the hand is a new perspective trend in hand surgery and oncology.

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## Clinical Outcome of Recurrent Myxofibrosarcoma

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### Objectives

Myxofibrosarcoma typically affects the elderly. It is notorious for its extreme invasiveness and high local recurrence rate, however, little has been known about the clinical course of patients with recurrent tumor. We retrospectively analyzed the clinical data of patients with recurrent myxofibrosarcoma to elucidate the clinical outcome.

### Methods

Since 1999, there were a total of 141 cases of myxofibrosarcoma treated in our hospitals and 36 patients developed local recurrences during their clinical course. Factors that may affect the clinical outcome were investigated.

### Results

There were 25 males and 11 females, and the age at diagnosis ranged from 48 to 90 years old (avg. 67.9). The follow-up period ranged from 5 to 210 months (avg. 61.2). Ten patients (27.8%) had their initial tumors in the trunk, and 26 patients (72.2%) in the extremities. The overall average time interval between the initial surgical treatment and the first local recurrence was 31.9 months. Although the difference was not statistically significant, the average interval was 29.4 months for 26 patients treated by surgery alone, while the combination of surgery and radiotherapy prolonged the interval to 38.6 months. Among 34 patients who underwent surgical treatment for their recurrent tumors, 20 cases developed second local recurrence, and the 3-year local recurrence free survival was only 10.9%. Patients with local recurrence underwent multiple surgical treatments for their local control, up to 8 times in our series (avg. 2.9). 11 patients eventually had amputation at the proximal part of their limbs. The oncological outcomes were 18 NED, 6 AWD, 9 DOD, and 3 DOOD.

### Conclusion

This study highlighted the difficulty in the management of local control for patients with myxofibrosarcoma. We cannot cure the patient by radiotherapy alone, however, we did observe a slight prolongation of the local recurrence free survival after radiotherapy, which led us to reaffirm the significance of the initial wide resection for the tumor. Furthermore, novel multidisciplinary treatment is needed to reduce the recurrence as well as to treat the recurrent tumors.

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## Oncologic Outcome of Chondrosarcoma

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**Introduction:** Chondrosarcoma is the second most common primary malignant bone tumor, yet proper diagnosis, surgical staging and management continue to present a dilemma to many orthopaedic oncologist. Surgery is the main treatment for these cartilaginous tumors.

**Materials and Methods:** Forty four patients of Kyungpook National University Hospital over a period of 1992 to 2011 who were diagnosed with chondrosarcoma of both axial and appendicular bones and treated surgically and a minimum of 18 months follow-up were retrospectively reviewed.

**Results:** Twenty four patients with either graded 1 or grade 2 conventional intramedullary chondrosarcoma were treated with extended curettage and adjuvant cryosurgery. One (4.2%) had local recurrence necessitating resection and endoprosthesis reconstruction. Four clear cell chondrosarcoma of the proximal femur were also treated with resection and joint arthroplasty with no local recurrence or distant metastasis. Twenty other cases of both pelvic and extra-pelvic lesions were treated with wide resection and several reconstruction procedures. Four cases had local recurrences and pulmonary metastases. The overall survival in this series was 90.9%.

**Conclusion:** Our experience is similar to other reports in the literature. Grade 1 and less aggressive form of Grade 2 chondrosarcoma can safely be managed with extended curettage. Wide resection and reconstruction, often entails a possibility of function loss, should be reserve for more aggressive lesions. The fate of Grade 3 chondrosarcoma consistently shows a very dismal result with high rate of distant metastases, ultimately leading to the patient's demise.

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**TREATMENT OF PULMONARY METASTASIS OF OSTEOSARCOMA***Pavlo Kovalchuk<sup>1</sup>, Anatoliy Diedkov<sup>2</sup>, Grigoriy Klymnyuk<sup>2</sup>, Sergiy Bojchuk<sup>2</sup>, Victor Kostyuk<sup>2</sup>**<sup>1)</sup> National cancer institute <sup>2)</sup>, Ukraine*

Background: Using up-to-date schemes of chemotherapy allows to achieve 60-75% survival rate in patients with localized osteosarcoma. 25-40 % of patients develop metastasis (95% of them are pulmonary) during first 3 years. Metastasis treatment consists of second line chemotherapy and surgical or radiation treatment.

Methods: 260 patients with localized osteosarcoma, 10 to 21 years old (median age 16.8), treated in National cancer institute (Kiev, Ukraine) between 2003 and 2010 were identified. 89 patients had pulmonary metastasis after the treatment. Metastasis were detected between 6 and 38 months after the treatment (median - 22.3 months). All these patients received chemotherapy including carboplatin 600 mg/m<sup>2</sup>, etoposide 300 mg/ m<sup>2</sup> by the scheme: 3 neoadjuvant courses and 3 adjuvant courses with 21 day interval. Stabilization of the process was achieved in 61 patients (68.5%). 29 (33%) of them underwent metastasectomy, 60 (67%) patients were considered inoperable and underwent palliative radiation therapy (15 Gray on each lung). Metastasectomy was not performed because of the tumor progression despite chemotherapy or impossibility to remove all of the pulmonary metastasis. In 1 group 3 (3,4%) patients had one lung affected, 26 (29%) patients had bilateral metastatic affection (from 2 to 22 metastasis on each side). The single-step bilateral pulmonary resection was performed in 3 patients with bilateral metastatic affection, in 23 other patients metastasectomy was performed with the 10-14 day interval.

Results: 5 years overall survival was 12.4%. In surgical treatment group 5 years survival was 35.6%, in conservative treatment group – 1.7% (pConclusion: Prognosis in metastasis relapse of osteosarcoma depends on the response to chemotherapy and the possibility to perform surgical removal of the metastasis.

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## Intra-abdominal and retroperitoneal metastases in patients with soft tissue sarcomas - a two-center study

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**Background:** Intra-abdominal and retroperitoneal metastases are rare in patients with soft tissue sarcomas. The objective of this study was to evaluate the incidence of metastatic disease in these locations and to determine the optimal diagnostic approach.

**Methods:** The files of 613 patients with soft tissue sarcomas arising outside the abdominal cavity treated with curative intent between 2000 and 2009 were retrospectively analyzed. Mean follow-up amounted to 58 months (range, 3-148 months) for all patients and 70 months (range, 24-148) for surviving patients who did not develop any metastatic disease. Fisher's exact test was used to compare unrelated samples. Non-parametric analyses were performed with the Mann-Whitney U test. Survival curves were calculated with the Kaplan-Meier method and compared with the log-rank test. **Results:** 31 patients (5.1%) developed intra-abdominal or retroperitoneal metastases after a mean follow-up of 18 months (range, 1-100 months). 12.8% of patients with myxoid liposarcoma developed intra-abdominal or retroperitoneal metastases, compared to 4.4% of patients with other histologies, a difference which was statistically significant ( $p = 0.025$ ). There were no significant differences in mean tumor size between patients who did and did not develop intra-abdominal or retroperitoneal metastases (9.8 vs. 8.9 cm,  $p = 0.124$ ). The presence of metastases was discovered in routine tests in 26 of the 31 patients, while only 3 patients presented outside routine follow-up with abdominal pain, which led to the diagnosis of metastatic disease. There were no statistically significant differences in post-metastasis survival between patients who developed intra-abdominal or retroperitoneal metastases and patients who developed metastases in other localizations (25% vs. 34% at 5 years,  $p = 0.297$ ).

**Conclusion:** Patients with myxoid liposarcoma appear to have a higher risk for developing intra-abdominal or retroperitoneal metastases, compared to patients with other soft tissue sarcoma subtypes. As metastatic disease in these locations appears to be usually diagnosed in routine follow-up prior to the development of specific symptoms, routine imaging of the abdominal cavity of patients with myxoid liposarcoma during follow-up seems to be justified.

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## **Chondrosarcoma: Correlation between radiological findings and histopathological diagnosis concerning the grade of malignancy.**

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### **BACKGROUND:**

Chondrosarcoma (CS) is a malignant tumor that produces cartilage matrix. It is a very heterogeneous tumor with areas of different grade of malignancy within the same tumor.

CS can be classified into the following 3 histological grades:

I: low cellularity, prominent chondroid matrix

II: increased cellularity, prominent myxoid matrix

III: high cellularity, atypia, mitosis.

### **METHODS AND MATERIAL:**

A list with all the patients with the diagnosis of CS between 2004-2011 was provided by the archive of the Pathology Department at Sahlgrenska University Hospital in Gothenburg, Sweden. Patients with uncertain diagnosis or incorrect initial diagnosis of CS as well as cases with incomplete radiological imaging were excluded. Since CS is a very heterogeneous tumor and a needle biopsy may not localize the area of highest grade, only cases where open biopsy was performed, were included.

42 patients fulfilled the criteria for this study and their MRI and if available CT examinations were studied by a senior resident in general radiology and an experienced musculoskeletal radiologist. The location of the tumor, the size, the tumor borders, the signal on T1 and T2, the contrast enhancement as well as the presence of surrounding edema, bone destruction or bone expansion, periosteal reaction, cortical bone changes, calcifications, intralesional bleeding, necrosis, metastases, pathologic fracture, progress in size and recurrence were recorded.

According to the radiological appearance and with no knowledge of the histological grade, each tumor was classified as low-grade, intermediate-grade and high-grade malignant tumor in order to correspond to the histological grading mentioned above. The radiological grading of each tumor was then compared to its histological grading.

### **RESULTS:**

The results from the comparison will be presented.

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## **Surgical treatment of the liposarcoma: a single centre experience**

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Liposarcomas are rare and diversify from well-differentiated to myxoid and dedifferentiated liposarcoma. We retrospectively reviewed all patients with a liposarcoma out of the Vienna Bone and Soft Tissue Tumour Registry from 1970 to 2010. One hundred and fifty two cases were identified. For 110 patients complete clinical data and follow up were available. Of these 110 entities, 33 were graded as G1, 40 as G2, 28 as G3 and 9 other. The mean age at surgical treatment was 51,8 (range 19-77) years. Twenty three (20,1%) patients died after a mean follow up period of 3,6 (range 0,07 to 13,3) years. Sixteen patients developed metastasis (9 lung, 2 liver, 5 other). When death was considered to be the endpoint, the cumulative probability of ten year survival was 76,3%. The wide range in the survival analysis is expression of the subdifferentiation with different prognoses and requirement of different therapeutic strategies. Prognostic factors have to be identified in further studies.

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## **Aneurysmal bone cysts treated non operatively with sclerosant injections**

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### **Injections**

**Methods:** Between February 2010 and February 2012 we decided to treat all primary aneurysmal bone cysts presenting to our institution with serial intralesional sclerosant injections. Twelve such lesions were treated (femur/2, tibia/2, pelvis/4, fibula/2, humerus and ulna/1 each. All cases had a diagnostic biopsy. There were 7 males and 5 females. Age ranged from 1 – 35 years (median 13 years). Polidocanol was injected percutaneously into the lesion under image guidance as an outpatient procedure. Healing was assessed by serial radiographs and symptomatic improvement as observed by the patient. Opacification of the lesion with an increase in cortical thickening was taken as evidence of healing. Injections were repeated (maximum 4) at an interval of 6 to 8 weeks if the lesion did not show evidence of healing. If radiographs started to demonstrate evidence of healing and patient experienced symptomatic relief no further injections were given.

**Results:** All but one of the lesions showed evidence of healing. One lesion in the periacetabular area showed no evidence of healing after 3 injections and was operated with curettage and bone grafting. A 1 year old child needed surgery subsequently because of a progressive varus deformity developing at the site of the lesion. Four cases healed with a single injection, 2 had 2 injections, 3 had 5 injections and 1 had 4 injections. The first evidence of radiologic healing was seen from 6 to 24 weeks (median 12 weeks). There were no complications.

**Conclusion:** Though a longer follow up is mandated to rule out development of recurrence, early results for this inexpensive non invasive method of managing aneurysmal bone cysts are promising.

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## Osteoid Osteoma of the Pisiform, Leading to Misdiagnosis

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### Background:

Osteoid osteoma (OO) is an uncommon benign bone-forming tumor of the musculoskeletal system with uncertain etiology but it is the most common primary bone tumor of the carpal region, although much less frequently seen in the upper extremity. The most commonly involved carpal bones are scaphoid and capitate. OO of the pisiform has been reported only twice in literature. In this paper we present a rare case of OO of the pisiform which had not been detected in all diagnostic studies before the ultimate diagnosis was made 8 months later with the same diagnostic modalities and similar clinical signs.

### Case:

Our case is a 19 year-old male who had admitted to our institution with wrist pain. He had been evaluated clinically with imaging studies like MRI, CT scans and radiographies for 8 months before the diagnosis was made with the same imaging modalities for the second time. During the 8 months period he received conservative treatment for several provisional diagnoses like triangular fibrocartilage complex injury and arthritis, meanwhile none of the imaging studies showed a mass in the pisiform apart from medullary edema.

### Conclusion:

We presented a case of OO with absence of any detectable mass apart from medullary edema in the pisiform for about 8 months. After 8 months of follow-up, diagnosis of a newly formed OO in the pisiform was made as the source of complaints. Therefore, in cases with long standing ulnar wrist pain, even if diagnostic studies are inconclusive, one should consider osteoid osteoma in differential diagnosis and continue following the patient regularly in case an osteoid osteoma may become visible in the carpal region.

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## Granular cell tumors of soft tissue :A report of five cases

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### Introduction

Granular cell tumor (GCT) is a neural tumor characterized by large granular-appearing eosinophilic cells. Malignant GCT is an extremely rare, constituting 1-2% of all granular cell tumors. In 1998, Fanburg-Smith et al. proposed six histologic criteria for selection of benign, atypical or malignant. In this study, we classified our five cases according to Fanburg-Smith criteria. We also studied oncological outcome in these patients.

### Patients and Methods

Between 2000 and 2009, a total of five cases, who were finally histopathologically diagnosed as GCTs, were treated at our institution. The mean follow-up time was 77 months (32 to 162).

### Results

The mean age at diagnosis was 57 years (38 to 73). There were three male and two female. Of five patients, primary tumor sites were the forearm (n=3), the chest wall (n=1), and the thigh (n=1). All cases were treated by wide resection. According to Fanburg-Smith criteria, two cases were classified into benign, one atypical, and the remaining two cases were malignant. At the time of review, two cases with benign GCT developed no recurrence and no metastasis. The patients with atypical GCT developed local recurrence. One patient with malignant GCT developed no local recurrence and no metastasis but died from colon cancer and the other patient with malignant GCT developed local recurrence and metastasis, and died of malignant GCT.

### Conclusions

In our study, the clinical outcomes in our patients were related to prediction based on Fanburg-Smith criteria. However, some authors described that this criteria do not define all features of the disease in detail and evaluation of the positive features depends on each pathologist. We suggest that patients with GCT should be followed carefully, even if the patients were diagnosed as benign or atypical GCT histopathologically.

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## FIBRO-CHONDRODYSPLASIA OF PROXIMAL FIBULA. A BENIGN ENTITY TO CONSIDER IN THE DIFFERENTIAL DIAGNOSIS OF CHONDROSARCOMA.

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### Background

Fibro-chondrodysplasia or fibrocartilaginous dysplasia(FCD) is a variant of fibrous dysplasia(FD) in which extensive cartilaginous differentiation is identified. The amount of cartilage varies from case to case, however, no percentage has been proposed to consider this diagnosis.

In radiologic as well as macroscopic appearance, FCD is similar to a low-grade chondrosarcoma, but the key to a correct diagnosis is the histologic identification of the classical component of FD among of large lobules of cartilage, sometimes with increased cellularity and atypical chondrocytes.

We present an unusual pathology as FCD in an unusual location, proximal fibula.

### Methods

Seventeen-year-old boy with one-year history of growing mass in lateral site of the right knee and loss of External Popliteal Sciatic nerve (EPS) function. In another hospital they performed radiographs (Fig. 1) that showed a huge lucent lesion in the proximal fibula with popcorn densities and thin but defined cortex. MRI (Fig. 2) reported a 80x70x80mm lesion in proximal fibula, suggestive of chondrosarcoma, confirmed in a preliminary histological report of an incisional biopsy.

### Results

The patient was referred to our center for management and definitive treatment. The Sarcoma Committee reviewed the images and the histology, and the definitive diagnosis was FCD.

Due to complete paralysis of EPS nerve because of the tumor, we performed a resection of proximal fibula and reconstruction with calcaneus allograft screwed to proximal tibial and plasty of achilles tendon allograft for reinforcing the lateral ligament and avoid residual instability of the knee.

Currently, 4 months after surgery, the patient has a complete articular balance, and he recovered at the moment 1/5 of muscle strength in motor evaluation of EPS nerve.

### Discussion

First description of FCD was made by Pelzmann et al in 1980s. Series in literature reports few cases of FCD. More than 60% of the cases are in patients with polyostotic FD, and 27% of FCD cases had associated McCune-Albright syndrome.

Radiologically, FCD is well-demarcated and shows ground-glass opacity, stippled or ring-like calcifications suggesting cartilaginous malignant lesion. The cortex is always intact in spite of cortical expansion. The age of presentation ranged from 4 to 53 years. The proximal femur is the most common site of FCD. The differential diagnosis of FCD includes: enchondroma, chondrosarcoma, well-differentiated intramedullary osteosarcoma and fibrocartilaginous mesenchymoma.

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## Langerhans cell histiocytosis presenting spinal compression injury following vertebral fracture.

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### INTRODUCTION:

We report a rare case of multiple spinal Langerhans cell histiocytosis (LCH) with neurological deficits following vertebral fracture.

### CASE:

15-year-old boy had developing low back pain 2 months ago. He went to nearby orthopedic clinic and was seen conservatively. He could hardly walk with sensory disturbance of lower limbs 1 week ago. His neurological symptom was deteriorating rapidly. He was referred to our hospital by ambulance. He suffered from Frankel C neurological deficit of both lower leg with bladder and rectal disturbance. Plain X ray revealed vertebra plana of T4 due to compression fracture. CT showed osteolytic lesions in the T3-5 vertebra. MRI demonstrated extraskelatal tumor anterior to T3-5 vertebra and posterior protrusion of T4 which developed spinal cord compression. He underwent emergency laminectomy of T2-5, and partial tumor resection followed by posterior fixation using instrumentation of T1-7. His neurological symptom dramatically improved after the operation. Histological diagnosis was confirmed as LCH. Systemic examination revealed no other LCH except thoracic spine. As a result, he did not have lesion except for thoracic vertebra. He left our hospital 4 weeks after the operation. Systemic chemotherapy (VBL, PSL, 6-MP, MTX) was given. The patient shows no neurological symptom and no limitation of daily life, and imaging assessment demonstrates complete remission 1 year postoperatively.

### DISCUSSION:

LCH is a comparatively rare tumor and the annual incidence is reported at approximately 6 per million children per year. Multiple spinal LCH has been reported in only 55 cases in the literature review published in 2011, demonstrating that about 30% showed neurological symptoms. However, few had neurological deficits which required emergency surgical decompression as we reported here. Although the use of chemotherapy to treat LCH is still controversial, chemotherapy is commonly advocated for multiple spinal LCH. Radiation should not be used as first choice, especially in children, because of secondary malignancy and growth arrest.

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## Beware the ingrowing toenail: it could kill!

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**Background:** Pleomorphic liposarcoma, which accounts for 5% of all liposarcoma diagnoses, is an uncommon subtype of soft tissue sarcoma. Although this has been well described as occurring in the thigh, to our knowledge a high grade pleomorphic liposarcoma of the great toe has never been described in the literature.

**Patient and Method:** A 57 year old lady presented with a persistent, painless swelling of the left great toe which her general practitioner had been treating as an in-growing toenail for 5 years. Clinically, the mass encapsulated the great toe and invaded the first webspace and second toe. A diagnosis of grade two pleomorphic liposarcoma was made following assessment by magnetic resonance imaging and biopsy. The patient has since been treated with pre-operative radiotherapy and first ray amputation, with sparing of the second ray. A second resection showed no evidence of residual tumour within the foot.

**Conclusions:** Soft tissue sarcoma is a rare diagnosis, accounting for approximately 1% of all adult malignancies. As a result, an atypical history involving a growing soft tissue mass should alert the health professional to a potential diagnosis of soft tissue sarcoma. A high index of suspicion is required by clinicians when presented with a soft tissue mass in order to promptly diagnose and treat such a potentially fatal lesion.

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## Tenosynovial Giant Cell Tumour of the Knee - An Unusual Presentation

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**Background:** Tenosynovial giant cell tumours are classified as part of a set of rare proliferative tumours which arise from the synovium. These tumours are further divided by growth characteristic into Giant Cell Tumours of the Tendon Sheath (GCTTS) and Pigmented Villonodular Synovitis (PVNS), which have a combined incidence of 1.8 people per million. Pigmented villonodular synovitis is a diffuse tumour which more commonly affects the synovium of large weight bearing joints. Giant cell tumours of the tendon sheath, a localised tumour which forms a discrete nodule, involves the large joints including the elbow, hip, knee and ankle in only 12% of cases.

**Patient and Method:** A fit and well 27 year old female patient presented with a two year history of a popping sensation on kneeling or twisting her left knee, leading to patellar subluxation. After investigation using MRI and dynamic ultrasound a provisional diagnosis of a ganglion underlying the medial patello-femoral ligament (MPFL) was made. The patient developed an acutely locked knee and underwent an arthroscopic resection of the mass, which on histological analysis was found to be a giant cell tumour of the tendon sheath.

**Conclusion:** The authors have therefore demonstrated that the rarer variant of tenosynovial giant cell tumour is a differential diagnosis in patients with a solid mass within the knee joint. Any solid mass within the knee joint or atypical history should alert the surgeon to a possible soft tissue tumour.

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## Incidence and distribution of chordoma: A study analysing data from the "Surveillance, Epidemiology and End Results" program.

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### Background:

Only a few studies exist that describe the frequency distribution and incidence of chordoma, a rare tumor originating from remnants of the notochord. Apart from single-institution case series there are two bigger population-based surveys analyzing a number of 400 (National Cancer Institute, 1973-1995) and 409 (California Cancer Registry, 1989-2007) cases. With the use of the most recent dataset from the Surveillance, Epidemiology and End Results (SEER) program of the National Cancer Institute we conducted a retrospective analysis calculating distribution and age-adjusted incidence rates for 706 cases of microscopically confirmed chordoma from 2000 to 2009.

### Methods:

The Surveillance, Epidemiology and End Results program combines the information of 18 registries throughout the United States covering approximately 28% of the population. The WHO's "International Classification of Diseases for Oncology, 3rd Edition" morphological Codes for chordoma (9370/3 chordoma NOS, 9371/3 chondroid chordoma, 9372/3 dedifferentiated chordoma) were used to identify and include relevant cases. With the help from the SEER\*Stat statistical software, we calculated frequencies and age-adjusted incidence rates and analyzed them by gender, age, race, and primary site of presentation.

### Results:

The 706 cases are composed of 654 chordomas not otherwise specified, 46 chondroid chordomas and 6 dedifferentiated chordomas. The overall age adjusted incidence rate for chordoma is 0.09 per 100,000 and concerning gender it is higher in males (0.11/100,000) than in females (0.07/100,000; rate ratio: 0.61). The median age at diagnosis is 57 (range: 0-91) and the incidence rates increase with age. In blacks the incidence rate is with 0.03/100,000 significantly lower than in whites (0.10/100,000). Hispanics have a chordoma incidence rate of 0.08/100,000 in comparison to a rate of 0.09/100,000 in non-Hispanics. The distribution of the primary site of presentation is as follows: Cranial (42%, n=300); spinal (26%, n=182); sacral (30%, n=212); extra-axial, non categorizable and unknown site (2%, n=12).

### Conclusion:

With the use of the latest Surveillance, Epidemiology and End Results data (SEER18), which has been released at the end of spring 2012, this study provides substantial and up-to-date information on distribution and incidence patterns of chordomas in the United States.

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## Clinical and functional outcome of chondroblastoma of the bone - a single-centre experience with 44 patients

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Chondroblastoma is an uncommon benign bone tumour accounting for 1-2% of all primary bone tumours. 75% of chondroblastomas affect the long bones. Most lesions arise in adolescent patients between 10 and 25 years during epiphyseal growth. The main symptom leading to diagnosis is pain and local tenderness followed by swelling and limitation of motion. Treatment of chondroblastoma consists of curettage and bone grafting and provides local control in up to 82% of patients. The local recurrence rate after curettage has been reported with 10-35%.

We have retrospectively analysed our single-centre experience with 44 patients suffering from chondroblastoma of the bone (32 men; 12 women; mean age, 21 years; range, 11-58 years), affecting the femur in 17 patients (39%), the humerus in 12 patients (27%), the tibia in 5 patients (11%), (7%) the talus in 3 patients, the calcaneus in 2 patients (5%), and the os ischium, the os naviculare, the radius, the patella and the fourth toe in 1 patient each (2%). Pain was the most frequent symptom (66%). All but 2 patients were initially treated intralesionally by curettage and defect filling of the cavity. The mean age of surgery was 21 years (median, 18 years; range, 11 to 58 years).

Mean follow-up of all patients was 64 months (median, 26 months; range, 1-480 months). 4 patients were lost of follow up. In 3 patients (7%) minor complications occurred after surgery, consisting of wound healing disturbance, granuloma and haematoma. None of the patients developed a local recurrence. Functional outcome was assessed by the MSTS Score. The mean MSTS score of the upper limb was 99% with only one patient having a functional deficit. The mean MSTS score of the lower limb was 99% (median, 100%, range, 92% - 100%). 80% of patients had no functional deficit. We conclude that chondroblastoma can be cured in up to 100% with aggressive curettage and defect filling. This technique leads to excellent functional outcome and long-term control. Therefore we may conclude that surgery more aggressive than curettage is not warranted for the treatment of chondroblastoma.

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## **Ewing's sarcoma- regression grade I, but viable pulmonary tumor embolus. A case report.**

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### **Introduction:**

According to the literature, a regression grade I after neoadjuvant chemotherapy for Ewing's sarcoma has a strong correlation with a better survival rate. Nevertheless, even in this group metastases occasionally occur. We report a unique case of a 16-year-old male patient with a viable pulmonary tumor embolus despite a regression grade I after chemotherapy and resection of a Ewing's sarcoma of the chest wall (Askin's tumor).

### **Case presentation:**

At diagnosis, the Ewing's sarcoma showed a size of 7x5.9x6.9 cm in the MRI. The patient received six cycles of induction chemotherapy according to EWING 2008 protocol, leading to a massive reduction in tumor size (3.3 x 1.8 x 2.8 cm) in the MRI, followed by a wide resection of the tumor. During surgery, the surgeon felt a part of suspicious coarse consistency in the pulmonary lower lobe with less than 1 mm in diameter that he removed too. The histological examination of the surgical specimen of the thoracic wall revealed that there was no viable tumor tissue, according to regression grade I after Salzer- Kuntschik. But in the resected lung specimen, a small arterial vessel with a microscopic accumulation of viable immature, highly atypical cells in the lumen was found. Based on immunohistochemistry (FISH did not work) the diagnosis of a tumor embolism with vital Ewing's sarcoma cells was made.

### **Discussion:**

This puzzling finding led us to the question, how tumor cells could survive despite the excellent response of the primary tumor to chemotherapy. We speculate that a different microenvironment could be a possible cause. Other similar observations could lead to a better understanding of the tumor's metastatic potential.

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## Rare primary vertebral epithelioid angiosarcoma: a case report

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### Background

Primary malignant vascular tumors of bone are very rare. The epithelioid angiosarcoma is a high-grade sarcoma that is extremely rare in spine location and presents unpredictable clinical course. Frequently it is delayed or misdiagnosis, and presents a high metastatic rate and poor prognosis. In literature, metastatic bone angiosarcoma is invariably fatal.

The diagnosis is histological and immunohistochemical confirmation is important.

There are only few cases described of vertebral angiosarcoma. The main treatment is surgical wide en-bloc resection with or without adjuvants.

### Case Report

A 68-years-old male presented insidious low back pain in association to motor and sensitivity deficits, neurological gait claudication and weight loss.

An osteolytic lesion at the third lumbar vertebral body was analysed and characterized.

The PET scan showed an intense uptake at L3 and a slight uptake at the joint of the sixth dorsal vertebra with the rib that presented no tumor characteristics at the MRI.

A Tru-cut needle biopsy CT-guided revealed inflammatory tissue at the sixth dorsal vertebra and was compatible with primary epithelioid angiosarcoma of L3.

It was a type 5 of Tomita spine bone tumors classification, with paravertebral extension.

Tumor resection with total vertebrectomy of L3 was performed posteriorly. The surgical reconstruction consisted in posterior pedicle screw instrumentation of L1-L2-L4-L5 and interposition of a titanium expandable cage filled with iliac bone allograft and added a cross-link.

The histopathology and immunohistochemistry of the resected tumor confirmed a high-grade epithelioid angiosarcoma.

The prognostic was extremely poor due to the paravertebral extension of this malignant aggressive tumor. He recovered sensitivity deficits but persisted paraparesia. Then, he presented a *Pseudomonas Aeruginosa* nosocomial sepsis with urinary tract starting point. The patient died within 1 month postoperatively.

### Discussion

In literature, few bone epithelioid angiosarcomas are described and in spine location are extremely rare. They are a diagnostic and surgical challenge.

Although the total vertebrectomy performed the en-bloc resection was not possible due to paravertebral tumor extension. It showed an aggressive behaviour in association to morbidity and mortality.

Survival rate of these tumors is unknown but is essential an early diagnosis to allow a successful surgical wide resection.

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## MULTIFOCAL, METACHRONOUS GIANT CELL TUMOUR WITH RARE LOCALISATION AND METASTATIC SPREAD: A CASE REPORT

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**Background:** Giant cell tumour (GCT) of bone represents about 5% of primary bone tumours, but occurrence of multifocal GCT is rare. Herein, we present a case of a 59-year old male patient, who suffered from multifocal, metachronous GCT, which involved skull, os sacrum, lung and abdomen. **Case presentation:** A 59-year-old patient presented at our department with an osteolytic lesion in os sacrum in February 2012. In 2007 a lung tumour was found, suspected to be a carcinoma and treated by lobectomy. Further, in 2009 he was diagnosed for an osteolytic lesion in os frontale, which came out to be a GCT. After MRT and CT-scans of the sacrum it was decided to perform a biopsy at our department. The histological diagnosis from biopsy revealed a GCT. Therefore, the specimen of the lung from 2007 was questioned again and the differential diagnosis of metastatic GCT, due to a masked primary lesion, was brought up. Because of the patient's history it was decided to start systemic therapy with RANKL-inhibitor Denosumab. A few months after diagnosing GCT at the sacrum, a routine CT-scan of the abdomen revealed another lesion. Excision revealed the diagnosis of GCT. During a follow-up period of 6 months there was no progression of disease during therapy with Denosumab.

**Discussion:** GCTs of bone are classified as benign or intermediate neoplasm and mostly affect long bones. Multifocal GCTs occur in less than 1% of all patients and additionally metastatic spread is very uncommon. In our case the patient developed GCT in the skull and spine with an interval of 3 years and he also showed metastatic spread to lung and abdomen. Metastatic lesions of a masked primary GCT could be mistaken and could lead to other/wrong ways of therapy.

**Conclusion:** The present case report emphasizes the possibility of a multifocal GCT of bone as a possible differential diagnosis for multiple osteolytic lesions with metastatic spread to lungs, abdomen or other regions.

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## Recurrences and Functional Outcome after Therapy of Aneurysmal Bone Cysts

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### Background:

Aneurysmal bone cysts (ABC) are rare benign lesions, growing locally destructive, with a known tendency to recur. To cure the lesion an operation has to be performed. The aim of our study was to determine the rate of recurrences and the functional outcome of our patients.

### Methods:

Between 1981 and 2012 we treated 49 histologically diagnosed ABCs in 48 patients (22 female vs. 27 male). We performed 65 operations to cure the lesions. The patients were reviewed in regards to age, gender, size, localisation, the presence or absence of symptoms and fractures, number of operations, the applied operative procedures, the outcome and the rate of recurrences. The mean follow up was 36 months.

### Results:

Patients' age was at an average of 23 years. The average maximum diameter of the cysts was 4,95 cm. The lesions were mostly located in the lower extremities (48,98%) followed by the upper extremities (22,45%), the pelvis (14,29%), the spine (10,2%) and the stem (2,04%). We saw ABCs of the soft tissue in 3 patients, 3 of all lesions were secondary ABCs. Almost all of the patients were symptomatic at diagnosis (93,88%), another 4,1% presented with fracture. 17 operations on recurrences were performed in 14 patients (28,57% rate of recurrences), 4 of those patients had undergone a previous curative operation at another hospital. Multiple recurrences were seen in only 3 patients (6,12%), none of them had to undergo more than 3 operations to achieve healing or stable disease. Patients with recurrences were slightly younger than the average (20 vs 23 years). The biggest functional deficit seen was one patient with extensions deficit of 5 degrees in the hip joint, another patient had a minor hypaesthesia of the lower limb.

### Conclusion:

Even though ABCs are a locally destructive growing lesion, mostly of the lower limb, with a high tendency to recur and need for further operations, especially in younger patients, outcome is good and functional deficits are very rare.

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## Intraneural ganglion cyst of the ulnar nerve: A rare localisation

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**Background:** Intraneural ganglion cysts are very rare benign tumors. They also called nerve ganglion, intraneural synovial cyst, intraneural cyst, nerve sheath ganglion, intraneural mucoid cyst, intraneural mucoid pseudocyst or intraneural ganglion. These cysts are most commonly seen in the common peroneal nerve near the head of the fibula. They are less common in the ulnar nerve. These cysts can cause pain, swelling, different variations of sensory or motor deficit at the affected nerve territory.

**Methods:** Our case is 58 years old female who complained from pain, progressive numbness, tingling and weakness at the left hand. She denied having trauma to her left hand. During our physical examination we found that muscle atrophy, swelling at the lesion side. She has positive Froment's sign. She had no provocative signs of nerve compression at his elbow or wrist. Preoperative electromyogram findings suggested that acute - subacute almost complete denervation of the muscles innervated by ulnar nerve distal to the lesion. magnetic resonance imaging showed us 9.5X7 millimeters ulnar nerve sheath tumor. Ulnar nerve seemed thicker. Surgery was performed two months after the complaints onset. During the surgery ganglion cyst was carefully excised while avoiding any damage to the surrounding nerve fibers. Gelatinous material was encountered. Gelatinous material and wall of the cyst was sent to the laboratory for pathological examination. Pathological findings were consistent with ganglion cyst.

**Results:** After surgery her complaints; especially pain recovered rapidly. 8 weeks later physical therapy and rehabilitation has been started and continued for 15 days. Electromyogram was repeated 12 weeks after the surgery. Electromyogram findings were compatible with regeneration of ulnar nerve distal to the lesion and partial axonal damage.

**Conclusions:** The English literature on intraneural ganglions are limited to only a few case reports, making it difficult for us to diagnose and plan a treatment algorithm for intraneural ganglions. We suggest surgically nerve decompression and ganglion excision for intraneural ganglion cyst. Especially in patients who's presented with pain and rapidly progressive denervation findings at nerve territory, intraneural ganglion cysts should be considered instead of entrapment neuropathy.

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## Cortical Desmoid – Distal femur cortical irregularities mimicking Malignancies

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### Background

Cortical Desmoid are self-limiting reactive fibrous lesions, considered to be a variant of fibrous cortical dysplasia, which has benign biological and clinical behaviour.

These lesions have highly characteristic locations and radiologic pattern, which corresponds to a focal intracortical defect located at the posteromedial aspect of the distal femoral metaphysis, at the site of muscle insertion of the medial gastrocnemius or adductor longus. The radiological findings of this entity range from a slight loss of cortical definition, to a ragged spiculation with ill-defined borders, suggestive of malignancy (surface osteosarcoma).

It has been observed in active children between the ages of 3 and 17 (most commonly among 10-15 years old). It has been reported to occur in 11.5% of males and in 3.6% of females, 35% being bilateral cases.

Most patients are asymptomatic and don't have palpable masses, reason for which most cases are accidentally discovered in a knee radiograph performed for other reasons.

The authors aim to present two clinical cases of Cortical Desmoid lesions.

### Case Report

A 10 years old male and a 14 years old female were observed in the emergency department after knee trauma during sport activities.

Clinical examination showed a physical pasting on inner side of distal thigh, tender to pressure.

Radiologically, spiculated lesions were observed at the distal femoral metaphysis, proximal to the growth plate.

The cases were discussed in a multidisciplinary meeting between Orthopaedics and Radiology. To distinguish between benign and malignant disease, further imaging was done: contralateral knee Xray and bilateral knee MRI/CT scan showed very similar images at the end of both distal femoral knees; bone scan was normal.

The correlation of imaging with clinical findings allowed to diagnose desmoid cortical lesions and no biopsy was performed.

### Conclusion

Cortical desmoid is observed in children and adolescents at posteromedial metaphysis of distal femur, and has a highly characteristic location and radiologic pattern.

It is important to diagnose cortical desmoid as a variant of normal and thus avoid the need to perform invasive diagnostic procedures to exclude malignancy.

This entity doesn't need treatment, just clinical and radiological follow-up.

The prognosis is excellent and lesion disappears upon reaching adulthood.

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## Extraskelatal osteosarcoma: a single-center experience with 15 consecutive cases

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**Background:** Extraskelatal osteosarcoma represents an unusual soft-tissue sarcoma that historically is reported to be associated with very poor prognosis. The objective of this study was to use a prospectively gathered database to describe the characteristics and outcome of patients with this rare malignancy.

**Methods:** From a large sarcoma database at a single institution, 15 patients with histopathologically confirmed extraskelatal osteosarcoma, who were treated between 2002 and 2012, were analysed.

**Results:** The lesion usually presented as a deep, enlarging soft-tissue mass. The thigh (6 cases), the lower leg (5 cases) and the shoulder girdle (3 cases) were the most common anatomic sites. The mean age at the time of diagnosis was 52.3 years (range, 15.0 ,–€œ 79.0 years). There was a slight female predominance (female-to-male ratio 1,3:1). Histologically, all were high-grade osteosarcomas. In 14 cases (93.3%) wide resection margins were achieved, whereas amputation was necessary in two cases. In one case intralesional resection was performed due to the unfavourable site in the paravertebral musculature. In our series, only one tumour (6.7%) recurred locally and one metastasized within one year; five patients (33.3%) had distant metastases at presentation. The preferred metastatic site was the lung. Overall and disease-specific survival at 5 years was 61.9%, with a mean follow-up of 17.3 months (range, 0.6 ,–€œ 98.8 months).

**Conclusion:** Extraskelatal osteosarcoma is an uncommon, high-grade malignant tumour, associated with high risk of recurrence and potential metastases. However, in our series the survival rate was exceptionally higher compared with those reported in literature. The treatment should follow established guidelines for treatment of soft-tissue sarcomas with radical resection appears to be the best option for local control. Along with aggressive resection of pulmonary metastases cure can be achieved.

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## Primary solitary amyloidoma of the sacrum - a case report and review of the literature.

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### Background:

Primary solitary amyloidoma of the axial skeleton is rare. This tumor-like lesion may have a particularly aggressive appearance characterized by local deposition of amyloid and bone destruction that can result in segmental instability. The thoracic spine is most commonly involved, followed by the cervical spine. Here we report the case of a primary, solitary amyloidoma of the sacrum, its diagnosis, treatment, and outcome.

### Methods:

Case description and systematic review of the literature.

### Results:

A 64-year-old female with a history of several years of back pain presented with recent exacerbation of local pain, weakness and paraesthesia of the right leg and increasing difficulties in bladder control. Imaging studies revealed an osteolytic tumor of the sacrum with extradural extension and obliteration of the spinal canal. Histopathological diagnosis of a plasmacytoid amyloidoma was made by CT-guided needle biopsy. Intralesional resection, lumbo-pelvic stabilization and postoperative radiotherapy resulted in complete resolution of neurologic symptoms. One year after surgery the patient is free of local disease. Literature review yielded less than 30 cases of primary amyloidoma of the spine. Only two previous reports of amyloidoma of the sacrum were identified. To our knowledge, this is the first case of solitary amyloidoma of the sacrum treated with surgical resection, stabilization and radiotherapy.

### Conclusion:

Primary amyloidoma of the sacrum is extremely rare. Clinical presentation may be nonspecific. Imaging features are variable and can mimic malignant tumor growth. Definitive diagnosis requires histopathologic examination and immunohistochemic specification. Systemic affection must be excluded with cardiac MRI as well as colon and kidney biopsies. At the level of the spine and the sacrum resection is recommended in cases with extensive bone destruction and neurological symptoms. Intralesional resection with postoperative radiotherapy is associated with significant improvement of clinical symptoms and good local tumor control.

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## Rare, benign, angiomatous lesions

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### Background:

Benign, vascular lesions most frequently occur in the skin. However, some entities may involve deeper layers and all kinds of tissues and may develop in a disabling or life-threatening way. Three very rare conditions requiring challenging surgery are presented.

### Patients:

1. Mixed Type Vascular Malformation of the Right Lower Extremity and Pelvis. A 22-year-old female was seen in a poor condition with extensive swelling and bulging deformities of the right lower extremity. There were necrotic, infected ulcers of the foot. When the leg was lowered extensive bleeding would occur and when the leg was elevated pulmonary oedema would occur. The extremity was calculated to contain 6 liters of blood, important coagulation factors were continuously consumed in the lesion. An extended hemipelvectomy including the rectum was performed. At 17 years follow-up the patient had good quality of life and full-time work.
2. Multifocal Intraosseous Epithelioid Hemangioma. A 35-year-old man had an osteolytic lesion of the right distal radius diagnosed as giant cell tumor of bone. A resection arthrodesis was performed. At follow-up one year later an osteolytic lesion was detected in the second metacarpal bone and further surveys including PET-CT disclosed altogether 6 osteolytic lesions in the right upper extremity and right second rib. All lesions were excised or curetted and cemented. Three years later a lesion of the left side of the sacrum was diagnosed and excised. PET-CT proved to be the best imaging tool and is done at regular intervals.
3. Gorham's Disease (Disappearing Bone Disease) of the Thoracic Spine. A 37-year-old man had MRI because of back pain. An extensive osteolytic lesion of the T7 vertebral body was seen. Repeated transpedicular and finally open biopsies yielded considerable bleeding but no abnormal cells. Angiography showed no hyper-vascularity and no vessels to embolize. At this stage there was total absence of T7 and considerable osteolysis of T6 and T8. The diagnosis was clear. The patient had stabilizing surgery with an extendable titanium cage and anterolateral fixation with rods and screws. He is on Alendronat medication and the condition is stable at 2 years follow-up.

### Conclusion:

Benign angiomatous lesions may cause as challenging diagnostic and surgical problems as any sarcoma. The variety of orthopaedic tumor surgery and the need to learn about rare conditions is substantial.

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## Radiological Evaluation of the Hip Joint Following Endoprosthetic Replacement of the Proximal Femur

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### Background

Endoprosthetic replacement of the proximal femur with a bipolar implant is associated with an excessive load on the remaining acetabulum. In order to alleviate the extent of potential future damage to the hip joint as a result of this load, some surgeons routinely place an acetabular cup, an approach that considerably extends the time of surgery.

We evaluated the long-term postoperative radiological changes occurring around the affected hip joint in patients in whom an acetabular cup was not placed.

### Methods

Follow-up imaging studies of 26 consecutive patients who underwent proximal femur endoprosthetic replacement without acetabular cup placement and were followed for more than 2 years were retrospectively reviewed. Plain radiographs were evaluated for the extent of acetabular protrusion, degenerative changes, and heterotopic bone formation around the prosthetic hip joint.

### Results

Protrusion of the prosthetic head was documented in 6 patients (23%), degenerative acetabular changes in 4 (15.3%), and heterotopic bone formation in 8 (30.7%). However, only 4 patients (15.3%) had symptoms associated with these findings that required surgery.

### Conclusions

There is radiological evidence of some protrusion, articular degeneration, and heterotopic bone formation in patients who undergo endoprosthetic replacement of their proximal femur, but the extent of these changes and the lack of clinical symptoms do not justify the routine placement of an acetabular cup.

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## Doppler sonography from children with osteosarcoma and Ewing sarcoma

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### PURPOSE

To study of capabilities of ultrasonic method in the diagnosis of osteosarcoma and Ewing sarcoma in children.

### METHOD AND MATERIALS

Were analyzed the results of Doppler investigation of 28 children aged 9-17 years with malignant tumors: Ewing sarcoma (13 children) and osteosarcoma (15 children) located in the lower extremities. All cases were prospectively verified morphologically. X-ray, computed tomography and ultrasonography was performed in 100% of cases. To assess of the regional hemodynamics, the degree of vascularization of tumor and the state of major vessels we used color Doppler ultrasonography, power Doppler and spectral wave analysis.

### RESULTS

A comparison study of indicators of children with osteosarcoma and Ewing sarcoma did not reveal significant differences ( $p=0,07-0,40$ ), that at this stage allowed them to unite in one group. Blood flow in the common femoral arteries (CFA) affected and healthy limbs in these groups have been varied in quantitative characteristics. The curves Doppler of blood flow for CFA of the affected limbs in most cases have been with high amplitude and above zero line during the pulse cycle (Pict.). The volume blood flow of the CFA to the affected limb was  $885 \pm 324$  ml / min, and for a healthy limb -  $424 \pm 138$  ml / min (p

### CONCLUSION

Were obtained the doppler symptoms for osteosarcoma and Ewing sarcoma in children. The data obtained by using Doppler technique at the initial stage of diagnosis together with by X-ray methods will permit better identify patients with signs of malignant lesions of the lower limbs.

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## Less Radical Resection for Soft Tissue Sarcomas Combined with Chemotherapy and Acridine Orange Photodynamic Therapy Produced Excellent Local Control

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### Background:

A wide resection is an effective method to inhibit local recurrence and poor prognosis for soft tissue sarcoma (STS). But if tumors are in close to major nerves, vessels, it's sometimes difficult to resect with wide margin. We established a new surgical therapy as acridine orange(AO) therapy which is supported by photodynamic surgery(PDS) and radiodynamic treatment(RDT) to reduce the surgical margin. We performed AO therapy(AOT) to STS patients, and analyzed the clinical outcome of AOT.

### Methods:

69 high-grade STS patients were treated with AOT. We selected the patients for AOT by following criteria; 1) Tumors contacted with major nerve, vessels or joint; 2) MRI showed less invasiveness to normal tissues. Procedure of AOT is that; 1) less radical resection (marginal or intralesional resection) is performed; 2) additional microscopic curettage with ultrasonic knife under tumor visualization with green fluorescence is performed(AO-PDS); 3) after closure of surgical wound, 5Gy of X-ray is immediately irradiated(AO-RDT).

### Results:

The details were shown in Table 1. 10-year overall survival(OS) and local recurrence free survival(LRFS) was 64%vs.68%. The average of ISOLS/MSTS limb function score was 93%, which indicates excellent limb function. In univariate-analysis, the following parameters influenced the OS: tumor size>5cm (Hazard-Ratio (HR)=1.12) and AJCC IV(HR=24.2). The LRFS was influenced by tumor size>5cm(HR=1.12) and effectiveness to preoperative chemotherapy(P-chemo) (HR=5.45). Intralesional margin status wasn't influenced for OS and LRFS. 10-year LRFS with or without P-chemo was 80% and 57%. Of 35 P-chemo patients, 17 showed the good response, and 10-year OS and LRFS of P-chemo responders were 91% and 92%. The factor of P-chemo response influenced the OS and LRFS significantly.

### Conclusion:

Although AOT has several limitations, AOT showed acceptable results in local control, prognosis, and limb function. Furthermore, the combination with effective P-chemo and AOT produced excellent results of OS and LRFS, even if the tumor resected with intralesional margin. All patients received AOT displayed excellent function, since AOT allows preservation of normal tissues. Based on the clinical outcome, we believe that AOT is useful for preserving excellent limb function with low risk of local recurrence, especially in chemo sensitive STS as rhabdomyosarcomas or synovial sarcomas.

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## The Feasibility of Irreversible Electroporation for the Treatment of Bone Tumor

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### Background

Irreversible Electroporation (IRE) is short wave of electric pulses can ablate undesirable tissues by generating nanopores on the cell membrane. Cells of the targeted area were ablated while preserve the vital structure like blood vessels and nerves. The non-thermal characteristic of IRE has been shown to exhibit numerous benefits over other traditional ablation technique and has been tested in humans for lung, prostate, kidney, and liver cancers. The effects of IRE are primarily dependent on the local electric field to which the tissue is exposed. Most of the tested tumors are homogeneous, for which the local electric field can be easily predicted. The effect on heterogeneous tissue such as bone tumor remains uncertain. In order to verify the effectiveness of irreversible electroporation's ablation on osteosarcoma, we evaluated the feasibility of IRE against bone tumor both In vitro and in vivo.

### Methods

**In vitro :** The osteosarcoma cell line SOSP-9607 were cultured, collected and then resuspended in normal saline solution was placed in a 4mm gaps parallel aluminum plated Gene Pulser Cuvette. IRE was performed on the cell suspension at voltage of 100 to 1500V, pulse duration of 100  $\mu$ s. Cell suspension was collected and Cell viability was determined with CCK-8 assay, LDH assay and typan blue stain.

**In vivo :** We established an osteosarcoma rat model, when the diameter of the tumors reached nearly 1.0 centimeters, IRE was applied to ablate the tumor. Rats were killed immediately, 3 days, and 1 week after IRE. The tumor tissues were processed for gross morphology and histological analysis.

### Results and Conclusion

**In vitro :** IRE can completely destroy osteosarcoma cell SOSP-9607. There was no tumor cell proliferation after continuous incubation 24 hours.

**In vivo :** Tissue histological examination post-IRE treatment revealed an extensive necrotic area. The sarcoma tumor cells got complete ablation.

In conclusion, our preclinical study shows the feasibility of IRE as a therapeutic modality to treat bone tumors.

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## **Bone substitutes and growth factors in the treatment of simple bone cysts: literature analysis and clinical experience**

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**INTRODUCTION:** The solitary bone cyst is a tumor like lesion typical of the immature skeleton whose etiology and

pathogenesis is unclear. Treatment depends on symptoms if they are present, the presence of a fracture, the size, the

location and the presence of cysts in an active phase.

**OBJECTIVES:** The literature shows many treatment options, often conflicting with each others. The purpose of this study is to perform a literature review focusing on the possible role of platelet gel to heal the lesion.

**METHODS:** The injection of substances such as methylprednisolone, autologous bone marrow, demineralized bone

matrix and calcium sulfate are the most used, but due to the high failure rate, often we use more aggressive surgical

techniques such as curettage, resection, associated with bone graft and, possibly, the intramedullary nailing.

**RESULTS:** We report two cases of lesions not responsive to injections of steroids treated with curettage and bone

marrow, platelet gel and bone substitutes.

**CONCLUSION:** In the bone cysts non responsive to minimally invasive treatment, curettage associated with platelet gel and bone substitutes represent a valid therapeutic option.

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## Can VAC therapy spread tumour cells all over the wound? The "buckshot" pathological pattern.

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### BACKGROUND

Soft tissue sarcomas represents a group of relatively rare neoplasms with a high number of histological subtypes. Still many difficulties exist in referring patients to a reference centre in order to have an appropriate and standardized treatment plan. The aim of this study is to present a case of incorrect clinical management with its pathological consequences.

### METHODS (CASE REPORT)

Female 79-year-old patient. Previous treatment (St Elsewhere Hospital): "hematoma" (without a proved hip trauma) aspiration in the trochanteric region, pathology report of high grade leiomyosarcoma, consequent open marginal-intralesional debridement without complete local and systemic stadiation, wound dehiscence treated with VAC therapy before final pathology report. The final report confirmed the diagnosis of high grade leiomyosarcoma with positive intralesional margins. After 2 months the patient was referred to the reference centre with a still open wound. A pelvis and lower limb MRI and a chest-abdomen CT were performed. Imaging showed no metastasis and a lesion extended 360° around femoral shaft along all the thigh and involving femoral neuro-vascular bundle and the cortical bone. The only possible surgical intervention was a hip disarticulation.

### RESULTS

The pathologist reported a multifocal "buckshot" dissemination of neoplastic cell clusters comparable to miliar diffusion in secondary tuberculosis. Considering the pathological examination the VAC therapy had spread cells in the anterior, posterior and medial compartments of thigh. Unfortunately CT chest after 3 months showed multiple lung metastasis.

### CONCLUSION

Many authors confirm that the use of negative pressure wound therapy after resection of musculoskeletal tumours is a safe and effective pathway to achieve wound healing after complications such as dehiscence, infection, or large soft tissue defect. This management is currently worldwide accepted. This experience confirms the strong suggestion to apply VAC therapy only after the pathological confirmation of clear marginal/wide margins. This case report unfortunately demonstrates that VAC therapy has the potentiality to spread malignant cells all over the open wound and that it must not be used in presence of active tumour tissue.

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## Restoring function after excision of the femur/humerus in primary bone tumors - Results with a “low cost” total bone prosthesis

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**Objectives:** Rarely, extent of tumor may necessitate resection of the complete bone to achieve adequate oncologic clearance in bone sarcomas. We present our experience with reconstruction in such cases using an indigenously manufactured low cost total femoral prostheses (TFP) and total humerus prostheses (THP). We assessed the complications of the procedure, the oncologic and functional outcomes and implant survival.

**Methods:** Twenty six patients, fourteen males and 12 females with a mean age of 26 years operated between June 2001 and October 2009 had a total bone replacement (8 TFP and 18 THP). The diagnosis included osteogenic sarcoma (12), Ewing's sarcoma (9), chondrosarcoma (5). Mean follow-up was 39 months (9 to 120 months) for all and 51 months (24 to 120 months) in survivors.

**Results:** There were 6 local recurrences and fifteen patients are currently alive at time of last follow up. The Musculoskeletal Tumor Society score for patients ranged from 16 to 25 with a mean of 23 (77%). The implant survival was 92% at 5 years with one TFP needing removal because of infection and one THP because of local recurrence.

**Conclusions:** A total bone prosthesis in appropriately indicated patients with malignant bone tumors is oncologically safe. Functional outcome is good using an implant that provides consistent and predictable results with low complication rates after excision of the total femur or humerus.

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## Intraoperative Photodynamic Detection of Desmoid Tumor Using 5-ALA

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### Background

Desmoid tumor is a locally aggressive benign lesion. High rates of local recurrence are attributed to difficulty in defining appropriate margins of resection during surgery. The authors hypothesized that uptake of a photosensitizing agent by the tumor cells would allow detection of remaining tumoral tissue in the surgical field.

### Methods

Between 2009 and 2010 the authors operated on 5 patients who had desmoid tumor. Patients were preoperatively orally given 5-ALA (20mg/kg). Following tumor resection, blue light was used to detect the presence of PPIX, the photoactive product of intracellular 5-ALA biosynthesis, in the resected tumor and within the surgical field.

### Results

All resected tumors demonstrated strong and positive fluorescence light, reflecting the presence of bioactive PPIX. However, such fluorescence was not present in the surgical fields.

### Conclusions

Residual tumor in the surgical probably cannot be directly viewed with the assistance of 5-ALA. However, assuming that microscopic disease is present in the surgical field, activation of the photosensitizing agent with a red light may induce tumor kill via formation of oxygen radicals and improve local tumor control following surgical resection.

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## BISPHOSPHONATES IN PREVENTING ASEPTIC LOOSENING OF MEGAPROSTHESIS

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**Background:** Aseptic loosening of megaprosthesis is the most common late complication of joint replacement and the reason of revision surgery. Instability arises in consequences of the absences of osseointegration at the contact between bone and implant surface with increased activity of osteoclasts. In this context the particular interest is the bisphosphonates drugs as inhibitors of bone resorption. Experimental studies have confirmed the impact of bisphosphonates on bone density around the implants, and the ability to initiate osseointegration in the area of direct contact of bone and implant surface.

**The aim:** To determine the impact of bisphosphonates on osseointegration of endoprosthesis legs at the clinical practice.

**Materials and methods:** 76 patients treated between 2006 and 2009 in Ukrainian National Cancer Institute underwent megaprosthetics with cement fixation. These patients were randomized into two groups depending on using bisphosphonates. The main group consisted of 36 patients and the control group of 40 patients, respectively. The following reconstructions were performed: distal femur - 27, proximal tibia - 22, proximal femur - 17, proximal humerus - 6, distal tibia - 4. The follow-up period ranged from 36 to 84 months (median follow-up period: 49.2 months). The mean age was 31.2 years. The analysis of the radiological signs of aseptic loosening of implant was conducted. Radiographic examination and evaluation of the following early radiographic signs: 1) the appearance of enlightenment site between stem and the inner surface of the cortex; 2) density decreasing of cortical bone; 3) dislocation of prosthetic legs. Bisphosphonates (pamidron acid 60 mg or zoledronic acid 4 mg) were administered once every two months after the operation for one year.

**Results:** In the control group the radiographic signs of aseptic loosening of prosthesis were observed in 5 (12.5 %) of 40 patients. One of them underwent endoprosthesis proximal femur replacement, other 4 patients with distal femur replacement. 4 patients demonstrated appearance of radiographic signs of aseptic loosening of prosthesis legs in the first year of follow-up, and 1 patient in the second year follow-up, respectively. In the experimental group the radiographic signs of aseptic loosening were observed in one case (2,8%) in the second year follow-up.

**Conclusion:** These results lead to a preliminary conclusion about the ability of bisphosphonates to decrease incidence of aseptic loosening of megaprosthesis with cement fixation. (This study is ongoing).

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## Histological Assessment of Pelvic Osteosarcoma after Heavy Ion Radiotherapy – a report of two cases

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### Background

Surgical treatment of pelvic osteosarcoma is difficult. We present 2 cases in which time-dependent histological assessment of pelvic osteosarcoma was performed after heavy ion radiotherapy.

### Cases

Case 1 was of a 14-year-old girl and Case 2 was of a 30-year-old woman. Both the patients presented with sacral osteosarcoma. They were diagnosed on the basis of the findings of needle biopsy. After chemotherapy, they underwent heavy ion radiotherapy. Thereafter, histological observation was performed using needle biopsy.

### Result

#### Case 1

Four months after heavy ion radiotherapy, extensive necrosis was still observed on histological examination, and the osteosarcoma was classified as Grade III/IV according to Rosen & Huvos classification. The observation further revealed lung metastasis, and thus, chemotherapy and lung tumor excision were enforced. Histological analysis of the lung tumor revealed viable tumor cells, and the tumor was classified as Grade II/IV according to Rosen & Huvos classification. Fifteen months after heavy ion radiotherapy, viable tumor cells were still observed, suggesting a recurrence. Twenty-one months later, the patient died of respiratory failure due to increasing pulmonary metastasis.

#### Case 2

Three months after heavy ion radiotherapy, fibrosis with scattered atypical cells was observed on histological examination. Even this patient showed lung metastasis, and thus, underwent chemotherapy and lung tumor excision. Viable tumor cells were observed on histological examination of the lung tumor. Twenty months after heavy ion radiotherapy, viable tumor cells persisted. However, imaging studies showed no increase in the volume of the pelvic tumor. The patient progress is being continuously monitored.

### Conclusion

We have presented 2 cases in which that heavy ion radiotherapy was believed to have good prognosis for pelvic osteosarcoma. We believe that heavy ion radiotherapy may be effective for treating pelvic osteosarcomas that are difficult to treat surgically.

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## The Impact Of Methotrexate and Tumor Necrosis On The Outcome Of Patients With Osteosarcoma.

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### Background:

Osteosarcoma (OS) is the most common non-hematologic primary malignant bone tumor. There are conflicting reports about the role of Methotrexate in the treatment and the role of histologic tumor necrosis as a predictor of survival.

We aim to show the benefit of Methotrexate in pediatric protocols, and the significance of tumor necrosis in predicting patient's survival.

### Methods:

Retrospective Chart review of all patients diagnosed with osteosarcoma from Jan 2003 to Dec 2009. Multiagent chemotherapy is used in all patients, while methotrexate is used only for pediatric patients. Results: Fifty-six patients with osteosarcoma were treated at our center during the study period. The median age of patients was 17.2 years (range, 6 to 51 years). A majority of the pediatric group (68%) and approximately half of the adult group (52%) received neoadjuvant chemotherapy as part of their therapy. One-fifth of tumors demonstrated greater than 90% necrosis with chemotherapy. Most resections (n=42, 75%) yielded adequate margins in both groups while the margins were involved in 3 patients and close in 11 patients. In the first 4 years, 29% of the patients with extremity tumors underwent LSS; while in the last period, 79% underwent LSS (chi-square test for trend, P=0.0001). For non-metastatic patients with extremity tumors, the 3-year EFS for children and adults were 67% ± 16% and 64% ± 20% (P=0.92), and for metastatic patients with extremity tumors, the 3-year EFS for children and adults were 32% ± 13% and 57% ± 16% (P=0.99). Necrosis (>90%) was a favorable prognostic feature with no events occurring in patients with good response (P=0.079). The 3-year EFS for patients with necrosis >70% was 83% ± 11% vs. 37% ± 10% (P=0.01).

### Conclusion:

Children did not have better outcome despite the addition of methotrexate. We found a marginal survival advantage at 90% necrosis; however, our study suggests that necrosis rates above 70% after neoadjuvant chemotherapy may be sufficient to indicate significantly better outcome.

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## Prevention of catheter-related infections in children with tumors of the musculoskeletal system

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**Background:** The treatment of musculoskeletal tumors in children requires numerous courses of chemotherapy that necessitate adequate vascular access. Implantable venous port-systems are free from many of the disadvantages associated with the use of external central venous catheters. Our goal was to reduce the occurrence of infectious and thrombotic complications in children with central venous systems.

**Materials and Methods:** From 2008 to 2012 we observed 281 patients with tumors of the musculoskeletal system aged 6 months to 17 years, for 147 (52.3%) of which implanted venous port systems were used and for 134 (47.6%) with external subclavian catheters. Estimated criteria: the development of catheter-related bloodstream infections and cases of catheter thrombosis. In cases of thrombosis, we injected the system with a 25,000 IU dose of urokinase with an exposure of 15 minutes. To seal the catheter between the usages, we used heparin or a solution containing taurolidin (no catheter-related infections were noted).

**Results:** Periportal tissue infection was observed in 3 cases (2.0%) of the patients with implanted venous ports, while the children with subclavian catheters puncture site infection was noted in 89 cases (66.4%). No catheter-related bloodstream infections were noted at children with venous ports. Thrombosis of venous ports was observed in 7 cases (4.7%), which caused by incorrect exploitation. The development of catheter-related bloodstream infections was noted in 18 cases (13.4%) at children with subclavian catheters. Subclavian catheter thrombosis was observed in 47 cases (35.0%). The treatment of complications caused in exploitation of a subclavian catheter required its replacement in 29 cases (21.6%), with the necessity of another general anesthesia. All venous ports worked satisfactorily. All cases of thrombosis were successfully treated.

**Conclusion:** The use of taurolidin solution to close the venous system in the intervals between treatments prevents infection. The treatment of catheter-related infections is more effective with a combination of taurolidin and urokinase, which provides lysis of the thrombus as a source of bacteria. The local use of a gel containing taurolidin at endoprosthesis infecting is possible. The number of complications is significantly higher in patients with subclavian catheters, which rises the risk of limb endoprosthesis infection.

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## CONSERVATIVE TREATMENT OF INOPERABLE GIANT CELL BONE TUMOR OF PELVIS AND SACRUM USING BONE RESORPTION INHIBITORS

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**Background:** Giant cell tumor is aggressive bone tumor. Surgical treatment is considered to be the only effective method of treatment of these tumors. The problem of primary inoperable patients with giant cell tumors is a challenge.

**Methods:** Between 2009 and 2012, a total of 5 patients had inoperable giant cell bone tumors of pelvis and sacrum at the National cancer institute in Kiev, Ukraine. Among them were 2 males and 3 females at the age from 19 to 32 years. Mean follow-up was 18 months (range, 5 to 38). 3 patients underwent bisphosphonates administration (zoledronic acid or ibandronic acid), radiation therapy and embolization of tumor-nutrient arteries; 2 patients received denosumab (monoclonal antibody blocking RANKL/RANK bond) by the scheme: 120 mg on 1, 8 and 15 day, then 120 mg once a month. The efficiency was assessed by clinical data: pain syndrome intensity, Brief Pain Inventory (BPI) questionnaire and CT scans comparison (volume and density of tumor).

**Results:** All 5 patients had pain syndrome intensity decrease after 1 week of study. Treatment with denosumab demonstrated more than 30% tumor regression. All of the patients are in remission status. 4 of them had tumor capsule density increase.

**Conclusion:** Administration of bisphosphonates and denosumab in patients with inoperable giant cell tumors of pelvis and sacrum is perspective, allows to achieve remission and to increase the quality of life by decreasing pain syndrome intensity.

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P14:101

## Immunotherapy based on dendritic cells is feasible for patients with malignant bone and soft tissue tumours

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### Background

Dendritic cells (DCs) are the most potent antigen-presenting cells of the immune system. They play an important role in the induction of a tumour-specific immune response and they may represent a promising tool in therapeutic vaccination against cancer. DCs immunotherapy was reported in some carcinomas, such as B-cell lymphoma, melanoma, prostate cancer, renal cell carcinoma and malignant glioma. But there are a few reports of DCs immunotherapy for malignant bone and soft tissue tumours in orthopaedics. To evaluate the safety and feasibility of autologous tumour lysate-dendritic cell (DCs) immunotherapy for patients with malignant bone and soft tissue tumours who failed other standard treatments.

### Methods

Twenty-five patients were enrolled and immunized with DCs. Patient tumours comprised seventeen bone tumours (osteosarcoma [10], chondrosarcoma [2], fibrosarcoma [1], angiosarcoma [1], metastatic bone tumour [3]) and eight soft tissue tumours (clear cell sarcoma [3], leiomyosarcoma [2], ependymoma [1], alveolar soft part sarcoma [1], MPNST[1]). Autologous DCs were generated *ex vivo* in the presence of granulocyte-macrophage colony-stimulating factor and interleukin-4. Solutions containing equal quantities of DCs pulsed with original tumour lysate (TL) and DCs pulsed with OK-432 were injected intradermally. Each patient received 2-5 x 10<sup>6</sup> cells one time a week for 6 weeks.

### Results

Immunizations were well tolerated by patients with only local redness and swelling at the injection site in four cases. Levels of interferon-gamma and interleukin-12 cytokines were increased after DC immunotherapy in seventeen patients, nine of whom subsequently developed delayed-type hypersensitivity against the tumour lysate or OK-432. At the final follow-up, four patients had stable disease and nineteen patients had progressive disease.

### Conclusions

Although improvement of clinical efficacy requires further research, toxicity-free immunization by tumour lysate- or OK-432-pulsed DCs is safe and feasible in patients with malignant bone and soft tissue tumours who failed standard therapy.

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P15:101

## Standardized Rehabilitation After Limb Salvage Surgery Improves Patients' Outcome

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### Background:

Limb salvage surgery (LSS) has become the treatment of choice for the vast majority of patients with primary sarcomas of the bone in lieu of amputation ; however, no published rehabilitation protocols are available for these patients, which can be important for improvement of function and decrease hospital stay as the case for hip and knee arthroplasty.

We have undertaken a pilot study to assess the feasibility of establishing a standardized postoperative rehabilitation protocol in the treatment of patients with primary bone sarcoma for the 5 major anatomical locations. ( Distal femur, Proximal tibia, Proximal and total femur, Humerus and shoulder girdle resections and Pelvic resections) , and show the applicability of this protocol.

### Methods:

All LSSs performed by orthopedic oncology surgeon and rehabilitation of all patients was based on a standardized rehabilitation protocol. Fifty nine patients received LSS in the above mentioned locations: endoprosthesis (n=49), bone allograft (n=5), or No replacement (n=5). Patients received limb salvage surgery for other locations were not included in this study.

Patient outcomes were measured using the modified Musculoskeletal Tumor Society International Symposium on Limb Salvage (MSTS/ISOLS) scoring system.

### Result:

The mean modified MSTS/ISOLS score for all patients was 87% (95% CI, 0.85,0.89), at a mean follow up of 24 months. The highest scores were for patients with distal femur =93% (95% CI ,0.91,0.95). Seven patients had interruption of more than 6 weeks in their rehabilitation and had a mean score of 71% (95%CI,0.64,0.82).

**Conclusion:** The proposed rehabilitation protocol is a comprehensive, organized, and applicable guide to be used after performing LSS at mentioned anatomical locations. Standardized rehabilitation resulted in improved patient functional outcome.

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## Novel Use of a Hip Spacer to Perform Reconstruction Following Extra-Articular Scapula Resection for Sarcoma

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### Background

Patients with high-grade scapula and peri-scapular sarcomas may be treated with either an extra-articular scapula resection (Tikhoff-Linberg procedure) or an intra-articular total scapulectomy. After such a resection, reconstruction of the remaining shoulder girdle must be performed. We present a case in which a hip spacer is used to perform the reconstruction following an extra-articular scapula resection for high grade spindle cell sarcoma.

### Methods

A 79 year old female presented with a mass increasing in size on the posterior aspect of her right shoulder. Computed tomography scanning demonstrated an expansile tumour in the region of the right scapula that had destroyed most of the blade. Ultra-sound guided biopsy indicated the lesion was a high-grade spindle cell sarcoma. There was no evidence of metastases on further imaging.

A Tikhoff-Linberg procedure of the right shoulder was subsequently conducted with en-bloc resection of the scapula, distal clavicle and proximal humerus. In order to reconstruct the shoulder girdle, a hip spacer (Spacer G by Orthodynamics) was cemented into the proximal humerus with the soft tissues tensioned appropriately. A synthetic mesh (LARS ligament by Corin) was then sutured over the prosthesis and secured to the osteotomised clavicular remnant and chest wall with non-absorbable sutures.

### Results

The patient made an uneventful post-operative recovery. The histopathological report confirmed a high-grade spindle cell sarcoma that had been completely excised with 2mm margins. Her wounds healed well with no complications and she retained very good hand, elbow and wrist function but no active motion of her shoulder.

Over three years following surgery she is alive and well, having been continuously disease free with no evidence of local or distant recurrence. Currently her Musculoskeletal Tumour Society Score (MSTS) score is 63 % and her Toronto Extremity Salvage Score (TESS) is 49 %.

### Conclusion

This case demonstrates that a comparatively inexpensive, readily available non-custom made hip spacer used in a novel way may serve to augment a definitive humeral suspension following a Tikhoff-Linberg procedure with a satisfactory result in terms of cosmesis, acceptance, distal upper limb function and disease free survival.

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## Serum metal ion concentrations following total knee arthroplasty using megaprotheses for tumour indications: Is there a matter of concern?

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**Background:** Metallic wear following endoprosthetic reconstruction is a continuing matter of concern in the literature. The aim of the study was to determine the values of cobalt (Co), chromium (Cr), and molybdenum (Mo) in the serum of paediatric patients following reconstruction of the knee using fixed hinge megaprotheses after tumour resection. Further, these metal ion levels were compared with pre-operative controls as well as metal ion levels following metal on metal (MoM) total hip arthroplasty (THA) and rotating hinge total knee arthroplasty with standard devices and megaprotheses.

**Methods:**

**Fixed hinge group:** There were ten patients with a distal femoral or proximal tibial device (Howmedica Modular Resection System/HMRS®). The mean follow-up was 109 months (range, 67 to 163).

**Rotating Hinge Knee groups (RHK):** There were 17 megaprotheses (Limb Preservation System; LPS/M.B.T.) and eight standard rotating hinge devices (S-ROM Noiles). The mean follow-up was 35 months (range, 9-67 months).

**Total Hip Arthroplasty group (THA):** Thirty-two patients underwent metal-on-metal large diameter total hip arthroplasty (ASR XL Head). For this study, the preoperative, the 12-months, and the 24-months data were regarded as controls.

**Metal ion analysis:** The concentrations of Co, Cr, and Mo were determined using electrothermal graphite furnace atomic absorption spectrometry (ET ASS).

**Results:** In the fixed hinge megaprotheses group the mean concentration for Co, Cr and Mo were 0,51 µg/dl (range, 0,04-1,28 µg/dl), 0,420 µg/dl (range, 0,148-0,891 µg/dl), and 0,06 µg/dl (range, 0,01-0,09 µg/dl). The values for Co and Cr were tenfold and twofold, respectively, increased compared to the upper values from the reference laboratory, while Mo was within the limits.

The serum concentrations of Co and Cr were significantly higher compared to the rotating hinge group with the standard device ( $p < 0.001$ ), and the preoperative controls ( $p < 0.001$ ), while the serum concentrations of patients following MoM THA were higher at one and two years of follow-up.

**Conclusion:** Determining the concentrations of metal ions following fixed hinge and rotating hinge total knee arthroplasty revealed significant increments for Co and Cr. Thus, periodic long-term follow-ups are recommended. Upon the occurrence of adverse reactions to metal debris or intoxications, the revision of the hinge implant to a rotating hinge device or another reconstruction method should be considered.

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## Tumors around the Hip Joint Treated with Resection Without Reconstruction. Report of 18 Consecutive Patients.

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### Background

Wide resection of large tumors of the proximal femur and acetabulum may require enbloc removal of the hip joint, which create a large bony defect associated with a considerable loss of function. Reconstruction of such defects usually requires the use of large metal implants. The authors chose not to reconstruct that defect selected group of patients and report their outcome.

### Methods

Between 1998 and 2007, 18 patients who had malignant tumors of the proximal femur and acetabulum underwent enbloc resection of their tumor with the hip joint. Reconstruction of the bone defect was not done because of either poor overall oncological or medical status. Following surgery, the operated extremity was put in a skeletal traction for a period of 3 weeks after which gradual weight bearing was allowed.

### Results

Compared with surgeries in which reconstruction with a megaprosthesis was done, the procedure done in the study patients was associated with a shorter operative time and less wound complications. Although a considerable limb-length discrepancy of 4-6 cm was documented in all study patients, all were able to ambulate with the use of assisting devices.

### Conclusion

Wide resection of the hip joint without reconstruction provides reasonable function and is associated with a lesser amount of surgical complications. It may be considered in patients who have a poor oncological prognosis or have an expected high risk of medical complications following a major operation.

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## Bilateral fibula graft - Biological reconstruction with after resection of primary malignant bone tumors of the lower limb

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**Background:** Biological reconstruction of osseous defects due to resection of lower limb malignant bone tumors aims at a permanent solution. This paper deals with bilateral vascularized fibular grafts (BVFG) as a method for reconstruction of metadiaphyseal defects of the femur and tibia in young patients suffering from malignant bone tumors of the lower limb.

**Methods:** This reconstruction technique was used in 11 patients (5 female, 6 male, mean age 14.0 years, femur n=5, tibia n=6) undergoing metadiaphyseal resection of lower limb malignant bone tumors between November 2000 and December 2011. The median length of the defect to be bridged was 16.0 cm (range 8-24.5 cm). In the six cases of tibial reconstruction, the ipsilateral and contralateral fibula was swivelled into the osseous defect. The fixation of the fibular grafts was achieved by standard plating. For the reconstruction of femoral defects, two free vascularized fibular grafts were used. All patients with an Ewing's sarcoma and an osteosarcoma had multimodal treatment according to the EURO-E.W.I.N.G 99 or COSS-96 protocol. Median follow-up was 63 months.

**Results:** R0 status was achieved in 10 cases. One resection of an adamantinoma resulted in an R1-resection showing no evidence of disease at follow-up of 12 months. None of the patients experienced local recurrence during follow-up. 2 patients died due to distant disease during follow-up. Full weight-bearing on the affected leg was permitted after a mean of 8 months (range 4–18 months). Complications occurred in five patients (bleeding from anastomosis n=1; fibular graft fracture (conservative treatment) n=1; infection and non-union n=1; plate failure and delayed union n=2). None of the complications led to failure of the biological reconstruction or to amputation. The MSTS scores was provided with a mean of 87% (range 67-100%).

**Conclusion:** Biological reconstruction of osseous defects is always desirable when possible. Good functional and durable results can be obtained using BVFG for the reconstruction of metadiaphyseal defects of the femur and tibia.

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## COMPLICATIONS ASSOCIATED WITH THE ARTIFICIAL BONE GRAFT SUBSTITUTE €žGeneX€

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**Background:** Artificial bone graft substitutes like GeneX, a tricalciumphosphate-calcium - sulphate - compound, are widely used to refill bone defects after curettage of benign tumours. At our clinic we observed severe postoperative complications after initiation of GeneX.

**Methods:** We designed a prospective single cohort study with 40 patients with bone tumours who should receive curettage and defect filling with GeneX. Due to serious postoperative complications the study had to be stopped after inclusion of 31 patients (11 male, 20 female). Mean age at operation was 40-years (range, 6-71). The lesions were located in the proximal humerus (9), the femur (7), the tibia (3) or fibula (2) and the small bones of hand (8) or foot (2). The tumour entities included 17 enchondroma, five simple/juvenile bone cysts and nine other benign bone lesions.

**Results:** Five out of 31 patients (16%) developed serious complications following surgery and GeneX refilling. Three presented sterile inflammation adjacent to GeneX and two developed inflammatory cystic formations (up to 15cm) in the soft tissue with time dependant growth regression. Of those three patients with sterile inflammation, two showed delayed wound healing and local pain, and the third needed revision due to severe skin damage.

**Conclusion:** In the current series, GeneX caused severe soft tissue inflammation and pain. Therefore, surgeons should be warned not to place this artificial bone graft substitute next to thin walled structures (erosion!), and further, to seal fenestrated bone carefully after curettage and defect filling. We state the notion that general mandatory detailed safety testing of artificial bone graft substitutes should be performed before market launch.

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## Resection of Malignant Chest Wall Tumors

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**Background;** We report about malignant bone and soft tissue tumors that performed chest wall resection.

**Methods;** Between 2005 and 2011, we performed chest wall resection on 9 patients (7males and 2 females) for malignant bone and soft tissue tumors. The average age at the time of operation was 58.6 (25-85) years old. Three cases were chondrosarcoma, two cases were MFH of soft part. Ewing's sarcoma, leiomyosarcoma, myxofibrosarcoma and MPNST were one case each. We investigated surgical methods, complications and prognosis about these cases.

**Results;** The average follow-up period were 32.0 (4-79) months. The number of resected ribs was one in one case, two in 3 cases, three in 3 cases, five in one case and seven in one case. For the case resected one rib and a case resected two ribs, we didn't reconstruct the chest wall and closed the wounds directly. For the other 7 cases, we performed reconstruction of chest wall with the expanded-polytetrafluoroethylene (ePTFE) mesh. Postoperative complications were aspiration in one case (resected 3 ribs), reinsertion of thoracic cavity drain in one case (resected 5 ribs), deferment of extubation and scoliosis in one case (resected 7 ribs). There was no case of infection to mesh. Local recurrences occurred in 2 cases postoperatively. The 5 years survival rate of the patients was 48.6%.  
**Conclusions;** Operations for malignant chest wall tumors are very invasive with open chest and unilateral intubation. In our study, postoperative complications didn't occur in the cases resected few ribs, and their postoperative course were good. In cases that resected a lot of ribs, we should pay attention to complications.

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## Functional outcomes after scapulectomy and reconstruction

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### Background:

Scapulectomy requires not only joint resection but also wide resection of the shoulder girdle muscles. Even the significance of reconstruction has not yet been determined because of the difficulties in comparing the different conditions. The purpose of this study was to investigate factors to influence functional outcomes after scapulectomy in multicenter study.

### Methods:

This retrospective study comprised 48 patients who underwent total or subtotal scapulectomy and followed at least one year after surgery. Patients were registered at Japanese Musculoskeletal Oncology Group affiliated hospitals. Soft tissue reconstruction for joint stabilization was performed when there were enough remaining tissue for reconstruction such as rotator cuff and tendons. In 23 cases, humeral suspension was performed. The average follow-up period was 61.9 months. Multivariate analysis was performed to patient's background to determine which factors influence Enneking functional score or active range of motion.

### Results:

The average functional score was 21.1 out of 30. Active shoulder range of motion was flexion 42.7, abduction 39.7, internal rotation 49.6 and external rotation 16.8. The amount of remaining bone influenced functional outcome, which means that preserving glenoid or acromion lead better function compared to total scapulectomy ( $p < 0.01$ ). Factors that influenced functional outcome include amount of remaining bone, soft tissue reconstruction, length of resected humerus, nerve resection, follow-up period, male, number of resected muscles, age, amount of bleeding ( $p < 0.05$ ).

### Conclusion:

Although shoulder function was almost eliminated following total or subtotal scapulectomy, minimal resection of bone and soft tissue reconstruction should lead to better function.

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## Shoulder arthrodesis reconstruction with a pedicled musculo-scapular crest graft after resection for bone tumor

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### Purpose of the study

En-bloc resection of proximal humerus leads to poor functional results when both deltoid muscle or axillary nerve and rotator cuff tendons have to be resected.

When stability and strength is preferred, arthrodesis might be proposed. We report a surgical technique for reconstruction of bone defect and shoulder arthrodesis with an homolateral pedicled musculo-scapular crest graft and its midterm functional results.

### Material and methods

Twelve patients underwent shoulder arthrodesis with this technique in order to reconstruct a proximal humerus bone defect. The aetiologies were malignant bone tumor resection for 11 patients (4 extra articular and 7 intra articular resections) and one extensive bone destruction after total shoulder arthrodesis. The mean length of the bony defect was 11.6 cm (6-15), and the graft bridged it in all cases, with an internal fixation by a plate. Function was evaluated according to MusculoSkeletal Tumor Society and Tess scoring system.

### Results

5 patients died from the disease 9 to 35 months after surgery. One patient recurred locally 11 months after resection and was amputated. Mean follow-up is 5.9 year (12 to 144 months). 9 patients healed without any further surgery. Three patients presented a non-union, with a local infection in one case. None of them healed after bone grafting, one patient is still alive with a distal non union. MSTS mean score was 71 % (63 to 80%) and mean Tess score was 70 (50 to 81). All young patients have a professional activity. No patients have sustained a decrease of functional performance after 1 year of follow-up.

### Discussion

This pedicled graft associated with internal fixation by plate leads to a similar or better rate of bone healing and functional performance compared to other techniques. Furthermore, it doesn't need microsurgical vascular sutures as when a vascularised fibular graft is chosen. Stability of clinical and radiological results with time is attractive for young patients. The limitation of proximal humerus resection is 15 cm in our experience. The patient must be informed of the poor cosmetic results even when augmentation of the graft by latissimus dorsi muscular flap is done.

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## Endoprostheses of proximal part of humerus after tumor resection

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**Background.** The replacement efficiency estimation of proximal part of humerus with metal endoprosthesis.

**Material and methods.** 30 patients with tumors of proximal part of humerus after resection are carried out replacement of humeral joint with endoprosthesis of an own design. Men - 17, women - 13. The age of patients varied from 16 till 55, on average - 25, 4 years old. All patients had a lesion of epimetadiaphyseal part by extent ion from 5 to 12 sm with scope from 1/3 to 2/3 semi-circles, with destruction of cortex. The presence of pathological crisis was not with contra-indications. Giant cellular tumor is revealed of 21 patients, 6 - chondrosarcoma, 1 - osteogenic sarcoma, 1 - angiogenic sarcoma and in 1 –metastatic lesions of the bone.

**Results:** the patients were observed from 4 months till 9 years. The functional condition of humeral joint was appreciated in 60 % patients as good, in 32 % satisfactory, at 8 % unsatisfactory. In observation term from 1to 6 months in 8 (26,6 %) were developed various type of complication: festering of postoperative wounds (4), postoperative osteomyelites (2) and formation of fistula (2). In observation term from 4 months till 3 years in 5 patients (16,6 %) the relapse of tumor, in 7 (23,3 %) - metastasis in remote organs (lungs - 6, cerebrum - 1) is revealed. From 30 patients 4 (13,3 %) died from progressing of disease.

**Conclusions:** Reliable, ideal method of replacement of bone defect after resection of humerus is endoprosthesis. The application of individual endoprosthesis for replacement of defect formed after resection of humerus, allows achieving preservation of operated extremity function.

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## Replacement of large joints in treatment of bone tumors

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**Background:** the analysis of results endoprosthesis of large joints in treatment of tubular bones tumors.

**Material and methods:** the analysis of results of surgical treatment in 154 patients who have been carried out by endoprostheses of large joints. 149 patients were with primary tumors and 5 with metastatic lesions, average age was 25 years. Men were 91, women - 63. By localization of tumor: in 21 case there was a lesion of proximal part of thigh bone, in 70 – distal part of femoral, in 28 – proximal part of shin-bone and in 35 – proximal part of humeral bone. By morphological structure, in 48 patients is revealed osteosarcoma, in 28 – chondrosarcoma in 1 – paraostal sarcoma, in 1 - reticulosarcoma, in 1 – angiosarcoma, in 1 – sarcoma of Ewing, in 68 – giant cellular tumor, in 6 – metastatic lesion.

Length of bone resection was from 8 to 24 sm.

**Results.** The complications have appeared in 32 patients (20,7 %), from them in 18 infections of lodge in prosthesis, in 14 instability endo prostheses, in 4 cases these complications were combined. In 11 cases infectious complications were stopped conservatively. Crippling operations in 4 patients, re – endoprostheses in-2, endoprosthesectomy with imposition of compression-destruction osteosynthesis in 1 patient are performed.

The reason of instability in 5 cases was loosing of endoptostheses legs in the marrowy channel, in 7 - destruction of design, in 1- reduction of construction (screw of articulated part), in 1- dislocations of the head of coxal prostheses. In 5 patients crippling operations, in 7 cases reendoptostheses, in 2 – reconstruction of endoprostheses are performed. A functional condition by scale MSTS: a knee joint - 76 % after resection of proximal part of shin bone and 91 % after resection of distal part of thigh bone, humeral joint - 75 %, coxal - 84 %.

**Conclusion.** Endoprostheses of large joints is an ideal and reliable method in surgical treatment of bone tumor provides the local control and allows receiving satisfactory functional results.

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## Risk of infection in oncological megaprosthesis reconstruction

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### BACKGROUND

Literature reports an incidence of Surgical Site Infections (SSI) in oncological patients undergoing prosthetic replacement, between 8% and 35% after implantation and 43% after revision.

The frequency of SSI has gradually decreased after the introduction of antibiotic prophylaxis, however the appropriateness of perioperative prophylaxis for these patients is still controversial.

The purpose of this retrospective study, conducted at the oncologic orthopedic Unit of G.Pini Institute in Milan, was to evaluate:

- the number of SSI in oncological megaprosthesis reconstruction between 2009 and 2011,
- possible risk factors associated to the onset of SSI,
- the antibiotic prophylaxis applied.

### METHODS

We reviewed medical records of patients who underwent clean megaprosthesis reconstruction and collected hospitalization and follow up data, focusing on possible risk factors implied in the onset of SSI: patient characteristics, duration of surgery, number of persons in the operating room, size of resection, blood losses, antibiotic prophylaxis, etc. We registered every SSI meeting the criteria set by the European protocol HELICS.

### PRELIMINARY RESULTS

86 surgeries were evaluated, 37 women (43%) and 49 men (67%) whose mean age was 48 years and mostly ASA 2 (43%) and 3 (39%). Administration of prophylaxis was usually recorded (95%) and continued postoperatively (96%) for an average of 8 days, often related to the length of postsurgical stay. Mean duration of surgery was 256 minutes with a mean of 7 persons attending the operating room. We recorded 6 SSI on 86 surgeries evaluated (7%): 4 deep and 2 superficial, 4 occurring after one month and 2 after one year from surgery. Statistical analysis will be completed by integrating data from year 2008, whose collection is in progress.

### CONCLUSIONS

The criteria for inclusion or exclusion set in this study, SSI definition and data collection forms, could be used in a prospective surveillance program, to be planned having made sure to be able to implement a follow up. Afterwards, the protocol could be improved and proposed for adoption in a prospective multicenter surveillance system.

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## Complications Following the Use of Megaprosthesis in Limb Salvage Surgery in Osteosarcoma; The Experience Of CCHE

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**Methods:** Starting in 2007 and till 2012, 178 cases of pediatric Osteosarcomas were treated at the CCHE. Among these, 57 (32%) patients were locally treated by limb salvage and reconstruction by megaprosthesis.

**Results:** The average age at presentation was 15 years (8-18) and the average follow-up period was 24 months (6 months-56 months). 34 tumors were located in the distal femur, 15 in the proximal tibia, 5 in the proximal femur and 3 in the humerus. 7 prostheses were of the expandable type. A total number of 18 (31.5%) complications were recorded at the latest follow-up. Complications included limited flexion and/or extension in 7 cases, 4 stem loosening, 3 cases of periprosthetic fractures, 2 cases of infection, 1 case of bushing failure and a final case of stem breakage. Five (27.7%) complications were treated conservatively and these included 2 periprosthetic fractures and 3 cases with limited range of motion. The remaining 13 complications required revision surgeries. No amputation was needed to manage complications. Both cases of infection were treated successfully with an average of 2 years of follow-up since last evidence of infection. Two patients who had loosening of their prosthesis returned to their daily activity with no further evidence of loosening or pain. The third patient died before treating her loosening. All cases of fracture healed completely and resumed full weight bearing and normal daily activity. Four patients with limited range of motion required admission to operative room. Two were treated by manipulation under anesthesia, one patient was treated by shortening of his prosthesis, and another, required revision of her entire prosthesis. Only this last patient remained stiff after surgery. The one case with bushing failure was treated by replacement with a new bushing and a case with stem breakage was treated by revision with a new prosthesis. At the latest follow-up, the average MSTS functional score was good (73.3%) with a minimum of fair and a maximum of excellent score.

**Conclusion:** Although the incidence of complications was high following megaprosthesis implantation and most complications required surgical intervention, management of such complications was usually successful and amputation was not needed.

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## Latissimus dorsi flap: old solution for coverage, new option to restore function

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### BACKGROUND

Latissimus dorsi flap (LDF) is a valid option to fill in big tissue defects after the excision of bone and soft tissue sarcomas of the upper limb. To substitute the function of a resected muscle is still challenging. The aim of this study is to evaluate the possible indications for a LDF either pedicled or free.

### METHODS

Fourteen LDFs have been performed from 2006 to 2012 at Orthopaedic Oncology Department CTO Hospital (Torino, Italy) in 14 patients (7 males; average age 52,5 years old, range 17-78 ys). The purpose of the flap (either coverage or functional), the characteristics of the flap (pedicled or free), the grafted area (upper or lower limb) have been evaluated. The function was measured comparing the function of the opposite limb.

### RESULTS

Six coverage LDFs (5 pedicled flap in the upper limb, 1 free flap in the lower limb) and 8 functional LDFs (6 in the upper and 2 in the lower limb) were performed. Functional LDFs substituted the deltoid muscle in 5 cases, the triceps, the quadriceps, the glutei in 1 case. The function was good in the upper limb except for the cases of associated bone resection and reconstruction; it was only fair in the lower limbs.

### CONCLUSION:

LDFs are characterized by low morbidity in the donor area, large amount of available tissue, easy harvesting with a trustworthy bundle. This study confirms the reliability of LDF as a coverage flap either pedicled or free. Even if good functional results were obtained in the upper limb, the possibility of using free LDFs to substitute a lower limb muscle (gluteus, quadriceps) is still debated. Where no other surgical options are available LDFs offer a strong and widespread reconstructive solution. Further studies are needed to clarify the use of functional flaps in reference centres.

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## Treatment of periprosthetic fractures in patients treated with a megaprosthesis after resection of a malignant bone tumour.

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### Background:

While tumour endoprosthetic reconstruction is the most common treatment after large segmental bone defects after tumour resection for primary and secondary bone tumours, periprosthetic fractures are extremely rare. However, accompanying chemotherapy, local radiation and long periods of non-weight bearing are compromising the bone quality significantly in a high percentage of patients. The treatment of periprosthetic fractures in tumour patients is extremely demanding. Osteosynthesis often fails due to the reduced bone quality and consolidation potential.

### Methods:

During January 2000 and Dezember 2012 we analysed 31 patients with periprosthetic fractures after tumour resection followed by reconstruction with megaendoprostheses. Initial diagnosis was predominantly primary high grade sarcoma, although 4 patients had bone metastasis of carcinoma. Chemotherapy was administered in 25 and local radiotherapy in 10 patients. The average patient age was 37,0 years. Fracture site was the humerus in 6, the femur in 16 and the tibia in 9 cases.

### Results:

Fracture occurred after a medium of 18.0 months after initial implantation. Cause of fracture was adequate trauma in 10 patients and inadequate in 21 patients (5x caused by tumour recurrence). Plate osteosynthesis was possible in 5 patients only. In 22 patients an exchange of the implant with an average bone loss of 7 cm (range 2-25 cm) was necessary. In 5 cases an additional joint replacement (2 x elbow joint, 3 x hip joint) was performed due to the absence of sufficient bone stock for a stem implantation. Recurrent sarcoma led to amputation in 2 cases. Complications were 2 periprosthetic infections requiring a two stage revision. One non-union after osteosynthesis was treated with an additional implant exchange.

However, finally all patients with limb salvage achieved full weight bearing in the latest follow up examinations.

### Conclusion:

Periprosthetic fractures in patients treated with tumourprosthesis are demanding. The common goal of treatment should always be the preservation of as much bone as possible for further revisions and an assessment of risks and benefits.

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## Complications Following The Use Of Megaprosthesis In Limb Salvage Surgery In Osteosarcoma; The Experience Of Children Cancer Hospital Egypt

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Starting in 2007 and till 2012, 178 cases of pediatric Osteosarcomas were treated at the CCHE. Among these, 57 (32%) patients were locally treated by limb salvage and reconstruction by megaprosthesis.

The average age at presentation was 15 years (8-18) and the average follow-up period was 24 months (6 months-56 months). 34 tumors were located in the distal femur, 15 in the proximal tibia, 5 in the proximal femur and 3 in the humerus. 7 prostheses were of the expandable type. A total number of 18 (31.5%) complications were recorded at the latest follow-up. Complications included limited flexion and/or extension in 7 cases, 4 stem loosening, 3 cases of periprosthetic fractures, 2 cases of infection, 1 case of bushing failure and a final case of stem breakage. Five (27.7%) complications were treated conservatively and these included 2 periprosthetic fractures and 3 cases with limited range of motion. The remaining 13 complications required revision surgeries. No amputation was needed to manage complications. Both cases of infection were treated successfully with an average of 2 years of follow-up since last evidence of infection. Two patients who had loosening of their prosthesis returned to their daily activity with no further evidence of loosening or pain. The third patient died before treating her loosening. All cases of fracture healed completely and resumed full weight bearing and normal daily activity. Four patients with limited range of motion required admission to operative room. Two were treated by manipulation under anesthesia, one patient was treated by shortening of his prosthesis, and another, required revision of her entire prosthesis. Only this last patient remained stiff after surgery. The one case with bushing failure was treated by replacement with a new bushing and a case with stem breakage was treated by revision with a new prosthesis. At the latest follow-up, the average MSTS functional score was good (73.3%) with a minimum of fair and a maximum of excellent score.

Although the incidence of complications was high following megaprosthesis implantation and most complications required surgical intervention, management of such complications was usually successful and amputation was not needed.

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## Does VAC therapy really promotes local recurrence of musculoskeletal tumors?

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Background: Vac therapy is widely used for treating open wounds in orthopedic oncology for better healing and to minimize the necessity for complex surgical interventions as free flap surgery or other prolonged plastic reconstructions.

We believe that the use of VAC therapy do not promote local recurrences.

Methods: From May 2004 to December 2012 we treated 30 patients with VAC therapy for open wounds .

in some case the wound was left open after primary surgery and in other group the treatment was for reopened wounds after infections or other soft tissue problems.

Results: The average treatment time was 10 days (7-22 days). In 15 patients the wound healed primarily with the VAC therapy and with no need for any further surgical treatment.

13 patients needed a simple skin graft for closure and 2 patients needed a muscle flap after the VAC treatment.

There were 3 local recurrences one after 2 month and the other two after more than one year.

Conclusion: According to our experience VAC therapy is safe to use in Orthopedic-Oncology patients. It does not promote local recurrence and recommended as adjuvant therapy for better wound healing and less extensive surgery.

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## SURVIVAL OF TUMOR ENDOPROSTHESIS

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**Background and Objectives:** Limb-salvage surgery has become the preferred surgical procedure for both aggressive and malignant tumors, as well some metastatic bone tumors of the extremities. Endoprosthetic replacement played a major role. The aim of this study was to evaluate the risk factors that may influence the survival outcome of the tumor endoprosthesis.

**Study Design:** Retrospective cohort study

**Methods:** Forty seven patients of Kyungpook National University Hospital over the period of 1991-2010 who had undergone tumor resection and endoprosthetic reconstruction, excluding pelvic tumor cases and a minimum of 2 years follow-up were retrospectively reviewed.

**Results:** Eleven patients had post-operative complications requiring endoprosthetic revision. Five had metal failure. Three had aseptic loosening. Two had periprosthetic fracture, while the last case had recurrent implant dislocation. One patient had infection but was controlled. We found statistical significance for extraarticular resection and proximal tibial resection as risk factors for subsequent revision. Kaplan-Meier survival analysis revealed significant differences in the survival curves in each variable. The overall 3 and 5 year survival rate for this series was 94% and 74%.

**Conclusion:** Our experience is similar to the other endoprosthesis survivorship reports in the literature. The long term survival of tumor endoprosthesis will depend on our understanding of the risk factors that may affect the outcome.

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## Venous thromboembolism prophylaxis in major sarcoma survey – Current Practice

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**Aims:** The risk of deep vein thrombosis and pulmonary embolism following major sarcoma surgery is not clear from the literature. Moreover some surgeons consider the use of chemical thromboprophylaxis causes major bleeding risk. The aim of this study was to assess the current practice of VTE prophylaxis worldwide.

**Methods:** A 5-question online survey was sent worldwide mainly to oncologists and orthopaedic oncology surgeons regarding their practice of VTE prophylaxis. Questions were designed to target ambiguous areas of VTE prophylaxis.

**Results:** Survey responses were received from many centers around the world. 85% used VTE prophylaxis while 15% used no prophylaxis. 42% used mechanical VTE prophylaxis while 82% used low molecular weight heparin. 30% used both mechanical and chemical VTE prophylaxis. The duration of the prophylaxis varied widely from few days to 10 weeks. Two thirds of the respondents felt that VTE prophylaxis benefit is more than the risk while one third felt otherwise. 10% felt that chemical VTE prophylaxis is a major bleeding risk for major sarcoma surgery.

**Conclusions:** The survey indicates wide variations in the current usage of VTE prophylaxis from major tumour centers around the world. It is important to identify that there is wide variation in the current practice before any consensus could be achieved. The findings of the study may also have medico legal implications for the justification of VTE prophylaxis.

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## Long term outcome of Endoprosthetic Replacement of the Proximal Humerus

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### Background

The proximal humerus is commonly affected by primary and secondary bone tumours. Developments in oncologic treatment strategies have resulted in a substantial increase in life expectancy and associated functional demands. The present study reports on the clinical outcome of proximal humeral endoprosthetic replacement using a modular implant.

### Methods

20 patients (male 6, female 14) were included in the study. We examined clinical outcome, patient and implant survival in patients with primary or secondary bone tumours. Patients were treated between November 2001 and December 2012 in a high volume sarcoma unit. Preoperative staging, tumour histology and grade as well as operative and adjuvant treatment was assessed. Postoperative complications, recurrence rates, and revision surgery were documented, as well as shoulder function was assessed.

### Results

Mean age at operation was 53 years (19-84). Histology revealed high grade osteosarcoma (n=4), low/intermediate grade chondrosarcoma (n=8), metastatic disease (n=5) and three cases of high grade soft tissue sarcomas affecting the proximal humerus. At final follow up, mean overall survival was 75%. In eight patients a gore-tex sleeve was applied to optimize soft tissue management. In four patients plastic reconstructive measures with free or local flaps were performed. Local tumour recurrence was noted in 3 cases, two of which were re-excised. Superficial infection appeared in one case, one patient developed deep infection which was controlled by single stage debridement and lavage. Furthermore, one case of revision surgery was performed because of recurrent glenohumeral subluxation. Functional outcome revealed mean forward active flexion of 23 degrees, abduction of 27 degrees and active external rotation of 33 degrees.

### Conclusions

The present oncologic cohort showed reasonable functional results after endoprosthetic replacement of the proximal humerus. Risk analysis showed acceptable overall and implant related revision rates. There are opportunities both at implantation in terms of surgical strategy, and moving forwards, in terms of implant design, for improved outcome in these difficult cases.

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## Strategies for Achieving Long-Term Stability of Proximal Humeral Reconstruction in Sarcoma Surgery

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**Aims:** Bony sarcomas of the proximal humerus often require complete resection of the humeral head as well as the rotator cuff apparatus. Options for reconstruction include free fibula with physis transfer and proximal humeral endoprostheses. Historically, dislocation has been the predominant problem with such operations. There are various surgical strategies which can be employed to stabilise the endoprosthesis. This paper critically appraises the surgical options available.

**Methods:** Twelve cases of bone sarcoma of the proximal humerus are presented in which various strategies have been used to stabilise the endoprosthesis. Patients were recruited sequentially into this observational study.

**Results:** Using a combination of these surgical strategies we have significantly reduced our endoprosthesis dislocations and have had an improved outcome in terms of patients TESS scores and functional outcome measures. We present the residual complications we have experienced, revision surgery where required, long-term stability and overall functional outcome.

**Conclusions:** Stabilising the proximal humeral replacement remains surgically challenging. There are, however, several strategies which can be employed to minimise the chance of dislocation. The relative pros and cons of the various methods including use of the MUTARS tube, pedicled muscle transfer, vascularised 1st rib transfer, coracoid interposition and glenoidplasty are discussed along with the relevant surgical techniques.

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## The successful use of a biologic graft for closure of anterior abdominal wall defect following excision of soft tissue tumour.

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### Introduction and Aims

Primary soft tissue tumours arising from the abdominal wall are uncommon. There are many surgical techniques available for abdominal wall repair following excision of the tumour, each having its own benefits. The options range from direct closure, to the use of tissue flap reconstructions and/or prosthetic meshes. Synthetic material like polypropylene mesh is a common choice for closure of the abdominal wall defect. This report outlines two successful cases of abdominal wall repair using the Cook Medical™ Biodesign® porcine intestinal submucosa biologic prosthesis.

### Methods

Two patients had excision of soft tissue tumours from the anterior abdominal wall. The soft tissue defect following the tumour excision was about 10x10 cm. The defect was primarily closed using a Biodesign® biologic graft.

### Results

The first case illustrates the closure of a 10x10cm defect secondary to excision of borderline myofibroblastic tumour of the anterior abdominal wall. The second demonstrates successful utilisation of the biologic graft in a patient with a BMI>30 who had undergone a previous right sided hernia mesh repair, presenting with aggressive fibromatosis measuring 7x7cm from the right iliac fossa. Both patients had an uneventful postoperative period with good wound healing and no infection. At the time of latest clinical review there is no evidence of recurrence of the tumour, seroma or hernia.

### Conclusion

Following excision of soft tissue tumours of the abdominal wall biologic reconstructions can be successfully used to bridge the defect with minimal morbidity.

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## Is Daptomycin a new key to solving the problem of Prosthetic Joint Infection?

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**The aim:** The aim of our study is to evaluate the possibility of using daptomycin in children and adults after implantation endoprosthesis.

**Materials:** There were 30 patients with cancer of bone, who underwent primary or repeat implant's replacement from 03.2010 to 05. Min. age 10, max. 48 years. Children under 14 used a dose 8-10mg/kg/day. Adults – 10-12mg/kg/day. Duration of the course in prevention of infection (due to the high risk of infection) varied introduction of 5 to 16 days. In the treatment of infection rate ranged from 14 days to 36. At high risk of infection, we mean: the patients with resection of the proximal tibia, with a deficit of soft tissue to cover the endoprosthesis, an extensive skin necrosis in the postoperative scar, reimplantation. At 1/30 (0.3%) patient developed an allergic reaction in the form of urticaria. For the treatment infection of the endoprosthesis bed daptomycin was used in 11 patients. Only in 8 out of 11 cases we had bacteriological seeding. In others cases – only indirect signs. In 6 out of 8 MRSE flora was detected, in 2 out of 8 - MSSA. Ineffectiveness of daptomycin revealed only one out of 8 patients - 12% with the agent of MSSA. In this patient during surgery revealed osteomyelitis-spoke - MSSA, for a long time to receive preventive therapy daptomycin 500mg/day - without effect, the patient was removed implant, the defect is replaced by a spacer from the bone cement with gentamicin - pus from the wound continues to stand out; bacteriological crops - without any flora.

**Result:** In all cases, the use of daptomycin for the prevention of infectious complications in high-risk after implantation, we have not received manifestation of any complications. In the case of the treatment of established infectious complications - efficiency was 10 of 11.

**Conclusion:** The use of the drug daptomycin in children and adults after using of tumor endoprosthesis, as a preventive antibiotic treatment is justified only for a group of patients at high risk of possible complications. Treatment of infections implant bed with daptomycin - effective, but requires further careful observation and analysis.

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## Successful reconstruction of total tibia and ankle joint with endoprosthesis. Experience for children and adults in East-European Sarcoma Group

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**Goal:** To this day, amputation is most widespread operation at distal tibia tumors. The purpose of our research is standardization of surgical treatment at such tumors for children and adults.

**Materials:** We report the clinical and functional outcome of limb preserving surgery and endoprosthetic reconstruction of the total tibia and ankle joint in twelve treated between 2008 and 2012 two of whom are children 12 and 15 years, respectively. Two patients underwent total replacement of the tibia: one for primary tumor, another for revision surgery. A mean age of 23 years, the most young patient was 12 years old.

We have used custom-made endoprosthesis of MUTARS® (Implantcast) and ProSpon. All stems of endoprosthesis have been fixed by bone cement with Gentamicin-3. All patients carried ankle joint orthosis from 2 till 6 months.

**Results:** Three patients developed a local recurrence and no patients – metastasis. We have not received any significant complications, such wound dehiscence or infection. MSTS score after 3 months was above 70%. MSTS score after 6 months was 78-82%. All were pain free and able to perform most daily activities. One patient with total tibia endoprosthesis still alive.

**Conclusion:** A custom-made endoprosthetic replacement of the total tibia and ankle joint is good treatment for patients with a primary bone tumour in quality to alternative of amputation. Now requires the development of new design prosthesis to restore the good function of the foot.

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## **Demanding limb salvage surgery operations in two «special» patients suffered of bone and soft tissue non Hodgkin lymphomas correspondingly**

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### Background:

Two «special» patients were diagnosed suffering of bone and soft tissue non Hodgkin lymphoma correspondingly were diagnosed on 2005 and 2011. The first patient (A), 37 years old man, single, very active, worker, presented a non Hodgkin Lymphoma in his tibia. He received treatment on 1989 for Ewing's sarcoma in his femoral bone. On 1991 he received chemotherapy together with radiotherapy for non Hodgkin bone lymphoma in his tibia. On 2001 recurrence in his tibia was diagnosed and treated with chemotherapy together with radiotherapy again. On 2005 he continued suffering of limited bone lymphoma and additionally of avascular necrosis of the tibia and of the supernatant skin, pathological fracture and osteomyelitis.

The second patient (B), 93 years old man, incredibly active -runner and jumper – at this age, diagnosed on 2011 with soft tissue non Hodgkin lymphoma of his right popliteal fossa.

### Method:

To the patient A chemotherapy was given followed by surgery. A vascular musculocutaneous graft from latissimus dorsi was developed and covered the skin necrosis. After the evaluation showed a vital skin graft, limb salvage surgery was performed in two stages. At the first stage the contaminated part of the tibia was excised, and cement spacer enriched with antibiotics was placed. Antibiosis for three months was given. At the second stage the cement spacer was removed and a long custom made joint sparing prosthesis was implanted.

To the second patient (B) because of his advanced age, light chemotherapy for 4 months offered after surgery and it was not easy to deal with the 93 years old neurovascular bundle of his popliteal fossa.

Result: The results five and two years post-op correspondingly are excellent according to MSTS and TESS scores and both patients are today very active without any recurrence or metastasis.

### Conclusion:

Limb salvage surgery is very demanding procedure and takes faith and knowledge from both the surgeon and the patient but really can change peoples life. The patient A is today married and a very happy father with three children and the patient B continues running and jumping.

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## **Malignant Pelvic Resections - The Blood (patient's), Toil & Sweat (surgeon's): Is it worth the effort?**

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**Aim:** Purpose was to evaluate morbidity, oncologic results and functional outcome in patients with malignant tumors of the pelvis treated with limb sparing resection.

**Methods:** Between March 2002 and November 2010, 106 cases of malignant pelvic tumors were treated with limb sparing resections of pelvis. Diagnosis was chondrosarcoma in 65, Ewing's sarcoma in 25, osteogenic sarcoma in 10, synovial sarcoma in 3, malignant fibrous histiocytoma, epitheloid sarcoma, and epitheloid hemangiothelioma in 1 each. Three patients had an erroneous pre-operative diagnosis of benign tumor and underwent intralesional excision; these were excluded from analysis. Remaining 103 patients underwent limb sparing resections with intent to achieve tumor free margins. Thirty eight patients had resections which did not involve the acetabulum and 64 had resection involving acetabular dome. Reconstruction was required in only 2 patients in whom resection did not involve acetabulum. For resections involving acetabulum various methods of reconstructions were used including pseudarthrosis, arthrodesis, extra corporeal radiotherapy – reimplantation and pelvic prostheses.

**Results:** Surgical margins were free in 83 patients and involved in 20. There were 3 peri-operative mortalities. Most common complications were wound related. Totally, complications were seen in 51 out of 103 patients (49%). Surgical intervention for complications was required in 26 patients (25%). Ten patients (9.7%) had a permanent complication related sequel, 9 had nerve palsy and 1 patient had a persistent sinus. 89 patients were available for follow up. The follow up in all patients ranged from 0 to 117 months (median 34 months). Nineteen patients (21.3%) developed a local recurrence. Fifty-eight patients are currently alive. Median follow up of survivors was 50.5 months (17-117 months). Overall survival at 5 years was 65.9% and disease free survival was 58%. Musculo Skeletal Tumor Society functional score was better in patients with acetabular dome sparing resection (90%) as compared with dome sacrificing resections (71.6%).

**Conclusion:** Though complex and challenging, surgery provides good local control and oncologic outcomes with acceptable function in these patients.

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## Laparoscopic assisted resection of an ileosacral chondrosarcoma

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### Rationale:

According to contributions of Yonamine we have begun to resect sacral tumors with video-laparoscopic exposure of the anterior structures.

### Patient:

A 33year old woman 6 weeks after her second normal vaginal delivery complained of lumbosacral dysesthesia. Imaging showed a mass of the sacrum crossing the ileosacral joint suggestive of a chondrosarcoma, after biopsy graded G1, calculated volume 700 cc.

### Technique:

The procedure was performed in an unstable lateral decubitus starting with the anterior laparoscopic exposure of the os sacrum and the right pelvic sidewall by passing through right pararectal space and full mobilization of the rectum from the promontorium downwards to the pelvic floor. After transection of the sacral hypogastric fascia, the medial and caudal limits of the tumor and as well as the sacral nerve roots were identified. The sacral nerve roots L5 - S2 attached on the tumor, while S3 and S4 were free. Full exposure of the pelvic ureter followed by the coagulation and transection of the internal iliac and the lateral sacral vessels. All cardinal vessels below the tumor were also transected including the pudendal and inferior gluteal vessels. The dissection of the lumbosacral space enabled the exposure of the lateral limits of the tumor and identification of both the obturator nerve and the sciatic just before it entry through the great sciatic foramen. 2 Gigli saws were inserted from anterior to posteriorly, one through foramina L5 and S1, the other through S1 and S4 for transection of the sacrum under visual endoscopic control. The resection of the ileum was performed in analogy to a Judet approach externally.

For reconstruction the defect was replaced with a massive allograft and stabilisation performed by lumbo-ischial screw and rod fixation.

The total blood loss was judged to be about 1000 cc; the total replacement were 2 units of blood.

### Results:

Pathologic examination showed uncontaminated margins.

### Conclusion:

We have got the impression, that the anterior video-laparoscopic approach presents several advantages by giving a superior view, higher precision and decreased blood loss for tumors in this anatomical difficult location of tumors.

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## Malignant bone tumors of the pelvis - biological reconstruction after surgical therapy

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Surgical treatment of malignant pelvic bone tumors can be very challenging. The objective of this retrospective study was to evaluate the oncological as well as the clinical and functional outcome after limb salvage surgery and biological reconstruction.

Methods: The files of 27 patients with malignant pelvic bone tumors, who underwent surgical resection at our department between 2000 and 2011, were retrospectively analyzed (9 Ewing's sarcoma, 7 Chondrosarcoma, 4 Osteosarcoma, 1 Synovial sarcoma, 1 Malignant fibrous histiocytoma and 4 carcinoma metastases).

Results: After internal hemipelvectomy reconstruction was performed by hip transposition (n=16), using autologous non-vascularised fibular graft (n=5) or autologous iliac crest bone graft (n=2). In four patients a femoral respectively a total hip prosthesis was implanted at the time of resection. The median follow-up was 33 months. 2 and 5 year disease-specific survival rates of all patients were 86.1% and 57.7% respectively. The mean functional MSTS score was 16.5 (~55%) for all patients.

Conclusion: On the basis of the oncological as well as the clinical and functional outcome, biological reconstruction after internal hemipelvectomy seems to be a reliable technique for treating patients with malignant pelvic bone tumors.

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## A Novel Approach in Endoprosthetic Pelvic Reconstruction

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### Introduction:

Mobile and durable reconstruction of the coxofemoral joint while avoiding limb-length discrepancy is a major challenge after periacetabular tumor resections. Massive allograft and megaendoprosthetic reconstruction procedures are being performed with usually unsatisfactory long-term results. We propose a new endoprosthetic reconstruction technique for internal hemipelvectomy, in which the ground reaction force is transferred to the spine through the shortest route possible.

### Methods:

We present our experience with 5 patients (M/F : 2/3) who underwent internal hemipelvectomy between 2005-2012. The mean age of patients was 29.4 (16-40) years. The mean follow-up period was 22 (3-52) months. The pathology was GII or GI-II chondrosarcoma in 3 patients, classical osteosarcoma in 1 patient and low-grade fibroblastic osteosarcoma in 1 patient. The pelvic resection was type I+II in two patients, I+III in two patients and II+IV in one patient.

The reconstruction was planned practically as a total endoprosthetic hip replacement. The acetabular components were implanted cementless with screw fixation at the proximal osteotomy site: sacroiliac joint in three patients, wing of sacrum in one patient and body of S1 vertebra in 1 patient. The leg length discrepancy was compensated with proximal femur replacement prostheses implanted cementless into the upper ends of femora through femoral neck osteotomy. Size 22 femoral head components were used. Capsular reconstruction was done with prolene mesh.

### Results:

Three patients were complicated by hematoma and prolonged drainage and one of them developed wound necrosis in the early postoperative period. These complications were managed successfully with debridement, vacuum-assisted closure and antibiotherapy. No prosthetic dislocation or loosening occurred. None of the patients required revision. One patient has radiographic finding of polyethylene wear. Mean MSTS score was 70%(50-80). One patient died of disease. Two patients underwent metastasectomy for pulmonary nodules. Two patients currently have no evidence of disease.

### Conclusion:

Although only short-term results are available, this technique has yielded outcomes comparable to those of other reconstruction methods. We believe this reconstruction to be biomechanically superior. However long-term results will be necessary to justify this assumption.

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## Possibility of using existing prognostic spinal scoring systems at patients with multiple myeloma and plasmacytoma

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### Introduction:

The aim was analysis of possibility of modern oncological prognostic scoring systems application at patients with multiple myeloma and plasmacytoma spinal column lesion.

Materials: Based on the comparative statistical analysis of the actual and expected survival rate at patients with multiple myeloma and plasmacytoma spinal lesions there was conducted the estimation of oncological Tokuhashi and Bauer prognostic scoring systems use possibility. In the Tokuhashi prognostic scoring system multiple myeloma and plasmacytoma was included in our study in the column oethers. Feature of the lymphoproliferative disorders is diffuse plasmacytic infiltration. Owing to what at a degree of metastatic assessment it was designated as absence. In analysis were included 48 patients with the diagnosis of multiple myeloma and plasmacytoma which were underwent with vertebroplasty and surgical treatment between January 2001 and December 2011.

### Results:

All patients having at the time of surgical treatment total score on a scale of Tokuhashi in the range of 12-15 that corresponds to life expectancy more than a year, endured this term. In group of patients who had a score before operation in the range of 9-11 and life expectancy more than 6 months  $88\pm 5,64\%$  of patients endured this term. In group of patients with estimated life expectancy less than 6 months  $50\pm 3,54\%$  patients achieve this term. Reliability of a scoring system made  $79,3\pm 4,69\%$ . In the real research all patients had an assessment on prognostic scoring system of Baur equal 3-4 middle term local control. Among 48 patients, 2 with the diagnosis of plasmacytoma was executed surgical treatment in volume of vertebrectomy and 11 (22,9%) palliative operations. In 73% of patients was carried mini-invasive surgery. This prognostic scoring system corresponds for 4,2% for the necessary volume of surgical treatment.

### Conclusion:

The received statistical results, allows to use Tokuhashi scoring system for prognosis of estimated term of life and volume of surgical treatment. Owing to absence in a scale of Bauer the column defining possibility to carrying out mini-invasive surgery and low it correspondence, the using it in a group of patients with spinal lesion by multiple myeloma and plasmacytoma isn't possible

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## En bloc vertebrectomy for the treatment of a spinal metastasis

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Spinal tumours account for 5% of all bone tumours. The spine is one of the most frequent sites of metastases.

Conventionally, curettage or piecemeal excision of vertebral tumors has been commonly practiced. However, clear disadvantages of these approaches include a high risk of tumor cell contamination of the surrounding structures and residual tumor tissue at the site due to the difficulty of distinguishing tumor from healthy tissue.

These factors contribute to incomplete resection of the tumor as well as high local recurrence rates of spinal malignant tumors.

According to Tomita et al, in the spine, one vertebra could be regarded as a single oncologic compartment.

The rationale of en bloc vertebrectomy is to allow a resection of the tumor in one piece together with a layer of healthy tissue (marginal or wide resection) and thus to reduce local recurrence rate and to improve long-term survival of the patients.

We present a case of a 16 year old female diagnosed with a spinal metastasis (T11), 2 years after having a resection and knee prosthesis for treatment of Ewing sarcoma of the left distal femur.

We performed a en bloc vertebrectomy of T11 using a single posterior approach, instrumentation from T9 to L1 with pedicle screws and reconstruction of the anterior column with an expandable cage.

Three months after surgery, the patient is doing chemotherapy. She has no pain or neurological deficit.

We present this case due to the rarity of a spinal metastasis from a Ewing sarcoma in the paediatric age, and because the procedure that was performed is a very demanding technique.

Until recently, the aims of surgical treatment were to reduce the neurological symptoms and improve the patient's quality of life. Total en bloc spondylectomy will not affect general metastases or extend survival, but if patients are carefully selected and if the operation is part of a total programme of management, this procedure may achieve local control of metastases and extend the patient's survival.

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P17:101

## Image based computer assisted surgery in curettage of bone tumors.

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### Introduction:

Intra-lesional treatment is a widely used surgical approach to benign and low grade malignant lesions like giant cell tumor, aneurysmal bone cyst, fibrous dysplasia and grade one chondrosarcoma.

Recurrence control is excellent with adjuvant therapy: either phenol/ethanol or cryotherapy. Intra-operative image assistance is usually proved with fluoroscopes.

### Method:

We have used images-based computer assisted surgery (CAS) as an alternative to fluoroscopes in 64 surgeries. Advantages of CAS are real time three dimensional feedback, higher resolution and better quality image datasets and no ionizing radiation. An instrument tracker is attached to the curette and registered during the CAS setup procedure. CT and/or MRI data is uploaded to the CAS system and fused if necessary, combing the characteristics of CT and MRI.

Fluoroscopy is still used for smaller lesions located in the diaphysis. CAS is also used for curettage after RFA, these have not been included. 26 cases have been analyzed where CAS was used in grade 1 chondrosarcoma without additional RFA therapy or with fibrous dysplasia. These cases had either large lesions (> 5 cm in diameter) or lesions located in a difficult anatomical location like the femoral head and pelvis. These lesions are often treated with segmental resections. All lesions were treated with phenol/ethanol, most reconstructions were done with PMMA.

### Results:

Average follow-up for the chondrosarcoma group of 21 lesions is 22,6 months (range 1-55), with 17 patients above one year of follow-up. In one cases there was a non complete curettage. MRI follow-up showed residue along the border of the resection. Pathological examination after re-do showed vital chondrosarcoma. For the fibrous dysplasia group follow-up is 28 months (range 6–58). There were no recurrences in this group.

Average lesion diameter was 7,6 centimeters (range 2,9–16,1). Locations were humerus (2), femur (20), tibia (2) and pelvis (2). There were five lesions in the femoral head/neck and two in the humeral head. There were two pathological fractures and one fracture after adequate trauma.

### Conclusion:

CAS can be an adequate replacement for fluoroscopes, especially in large or anatomically difficult locations. MRI before/after assessment and patient scoring is currently under analysis.

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## The first experience of intraoperational navigating system application at the resections of pelvic bones

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Now operations in the field of bones and pelvic joints are still insufficiently widely made. Difficult anatomic-topographical links of the pelvic bones and surrounding fabrics complicate the performance of radical operative intervention.. The first experience of the application of intraoperational navigating system in surgical treatment of patients with tumors of bones of a pelvic is presented in the country. The purpose: the introduction of highly technological methods of treatment at tumors of the pelvic bones.

Materials and methods: we represent the experience of the treatment of 20 patients with the use of intraoperational navigating system BrainLab from December, 2010 till December, 2012 in the clinic of general oncology 'The Russian oncological center of science of N.N.Blohin' of the Russian Academy of Medical Science. Age of patients is from 21 till 68 years (average – 37,2 years). There are 11 women and 9 men in the given group. The following resections are executed: 3 resections of the sacroiliac joint with combined bone grafting, 5 resections of iliac bone, 4 resections of pubic bone, 3 internal hemipelvicectomy, 5 resections of a sacrum. Histologically presented: 7 patients with giant cell tumor, 9 patients with chondrosarcoma of the II degree of malignancy, 1 patient with osteosarcoma and 3 patients with chordoma.

Radical operations according to the preoperative planning which were confirmed histologically were executed to all the patients. The accuracy of the resection performance varied from 1,2 to 1,8 mm. All the patients are alive without any disease signs through the given period of time. The duration of the operations was from 2,5 to 6,5 o'clock. The blood loss was from 700 ml to 3,5 liters (average - 2,5 liters).

Conclusions. The application of intraoperational navigating system raises radicalism of the treatment, considerably expands indications to the performance of safe operations on functionally significant zones, improving the results of the treatment and the quality of life

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## New hyperthermic treatment with magnetic materials for metastatic bone tumors

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### Background

Patients with bone metastasis in the extremities sometimes require surgical intervention to prevent deterioration of quality of life due to a pathological fracture. We have developed a new hyperthermic treatment modality using magnetic materials. The purpose of this study is to show the results of new hyperthermia for metastatic bone tumors.

### Methods

This new hyperthermic treatment modality was applied for 25 patients with 27 metastatic bone lesions. The age of the patients ranged from 27 to 80 years of age (median, 63 years), and the follow-up period ranged from 3 to 63 months (median, 11 months). The primary lesions included 5 lung cancers, 4 renal cell carcinomas, 3 hepatocellular carcinomas, sarcomas and breast cancer and others. Regarding the operation sites, 11 were the femur, 10 the humerus, 5 the tibia and 1 the fibula. In 10 lesions, after curettage of the metastatic lesion, calcium phosphate cement containing powdery Fe<sub>3</sub>O<sub>4</sub> was implanted into the cavity. For the 17 lesions, metal intramedullary nails were inserted into the affected bone. Hyperthermic treatment was performed postoperatively on days 8, 10, 12, 15, 17, 19, 22, 24, 26 and 29, using the newly developed electromagnetic field generator. The exposure time was 15 minutes per day. The radiographic outcome was evaluated at 3 months after surgery. The radiographic outcome was assessed according to following criteria. "Excellent" means a reduction of the lesion with visible bone formation. "Good" means no progression of the lesion for more than three months. "Poor" means a progression of the lesion. To evaluate the effectiveness of hyperthermia on radiographic findings, a univariate analysis was performed using the Mann-Whitney U test for non-parametric data.

### Results

On radiographs, 10 lesions (37%) showed an excellent outcome, while 16 lesions (59%) showed a good outcome and one lesion (4%) showed a poor outcome. No serious adverse effects were observed during the follow-up period.

### Conclusions

Our novel clinical hyperthermia modality using magnetic materials was thus found to achieve a good local control of metastatic bone lesions. Further investigations are needed before this technique can be employed as a standard therapy for metastatic bone tumors.

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## The use of modular Tumourprostheses in the Treatment of skeletal Metastases

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### Background:

Due to advancements in the treatment of carcinomas more patients reach the stage of bone metastases and survive several months or years in that stage. Thus the surgical treatment of bone metastases gets more important. One of the main aims of the surgical treatment is a long lasting reconstruction which survives the patient. Aim of this retrospective study was to evaluate the oncological outcome, treatment related complications and function after resection of metastases and reconstruction with modular tumourprostheses.

### Methods:

All patients were traced by our tumour database. Patient files were reviewed for clinical information. Additional information has been obtained using a questionnaire including the MSTS-Score. Between 1993 and 2008 we performed resection of metastases and implantation of a tumourprostheses in 82 cases (80 patients, 30 female, 50 male).

### Results:

The average age of the patients was 63 years. Most common primary tumours were renal cell carcinoma (46.7%), breast-cancer (21.3%) and lung cancer (7.5%). The proximal femur was affected in 45.1%, followed by the proximal humerus (25.6%) and the distal femur (17.1%). In 22 cases the tumourprosthesis was implanted as a revision due to local tumor recurrence or failure of the former osteosynthesis.

The mean survival after the operation was 2.9 years. The survival rate was 70% at one year, 20% at five years. The implant survival was 83% after one year and 74% at five years. The overall rate of operative revisions was 18%. Function and patients' contentment after operation is good (MSTS-score: upper extremity 67%, lower extremity 63%).

### Conclusion:

We show that the implantation of modular tumourprostheses can be an appropriate treatment for bone metastases. This operation has a low complication rate, patients rapidly gain a good function. Consistent with recent literature resection of the affected bone leads to an improvement of survival, especially in single metastases. Compared to other osteosynthetic devices the event free survival of the tumourprosthesis is high. Thus, even regarding the implant related costs, implantation of modular tumourprostheses might be the better option.

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## Scapular metastasis of a rectal gastrointestinal stromal tumor: a case report

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**Background:** Gastrointestinal stromal tumors are the most common mesenchymal cell originated neoplasms of the gastrointestinal tract with an annual incidence of 15-20 per million. Synchronous bone metastasis may be found with liver and peritoneal metastasis. However, based on our current knowledge isolated bone metastasis under Imatinib treatment has not been reported previously in the literature up to date.

**Methods:** A 53 year old male presented with a 2 month history of right shoulder pain that was not associated with a trauma. His physical examination revealed a palpable, painless solid mass that was not mobile at his right scapula and restriction of shoulder movements. He had a history of rectal GIST which had been subtotally resected nine years ago and postoperatively treated with radiotherapy and chemotherapy (Imatinib). Case was thought to be a distant bone metastasis and direct X-ray, Magnetic Resonance Imaging, Whole Body Dynamic Bone Scan and Positron Emission Tomography studies were done. WBDBS and PET/CT failed to show any evidence of skeletal or visceral metastases. After all these studies scapular metastasis of the GIST diagnosis was thought. Then this mass was excised totally (total scapulectomy) in the operating room by preserving axillary nerve. Pathologic findings of the material with the knowledge of the prior colonic malignant Gastrointestinal stromal tumor supported the diagnosis of Gastrointestinal stromal tumor metastasis. Treatment protocol of the patient changed to sunitinib therapy as the condition was accepted to be Imatinib resistant metastatic GIST. On the last control of patient there was no major side effect and an evidence of recurrence or metastasis.

**Results and Conclusion:** Up to date isolated bone metastasis of GIST under Imatinib treatment and after local control have not been reported in the literature. Regardless of the follow-up period, skeletal pain should be considered important and bone metastasis should be kept in mind for a GIST patient. Histopathologically, GIST bone metastases may be mixed with primary spindle cell bone sarcomas and differential diagnosis must be made by the demonstration of c-kit mutation with immunohistochemical methods. As in this case, metastasis may be at a rare location and mimic primary bone tumors.

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## **A Review of the surgical Management of Appendicular Skeletal Metastases and outcomes from a teaching hospital from the Mersey region.**

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### Introduction and Aims

The incidence of metastatic bone disease (MBD) is increasing. The aim of our study was to review the patients with Appendicular Skeletal Metastases who needed orthopaedic surgical management and their outcomes following the surgery.

### Methods

Between October 2009 and November 2012, we have identified retrospectively from our Trauma Database, 39 patients, who have undergone a total of 45 procedures on the appendicular skeleton. Variables investigated include: primary tumour; location of metastases; presence of pathological fracture; surgical treatment and outcome (survival).

### Results

There were 17 females and 22 males with an average age of 71.4 years at presentation. 38% (17/45 operations) of surgery was for a pathological fracture. The most common primary tumour was breast (12/45 operations) followed by lung and renal (both 7/45 operations). The femur was the most common site of metastasis (26/45 operations). Intramedullary nailing was the most commonly performed procedure (33/45 operations). 26 patients died with a median survival of 82 days (range 3 – 567 days). A subgroup analysis of patients with breast or prostate metastases showed that their median survival was only 81.5 days (range 5 – 441 days). A second subgroup analysis showed that a higher proportion of patients with pathological fractures died (81% vs 58% for prophylactic treatment) but the median survival was similar in both groups (81 days for pathological fractures, 82 days for prophylactic treatment).

### Conclusions

Our results suggest that absence of a pathological fracture or the primary tumours known to have good prognosis [breast, prostate] had no influence on the survival and the overall survival is poorer than expected.

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## PERCUTANEOUS TREATMENT OF UNICAMERAL BONE CYSTS WITH DEMINERALIZED BONE MATRIX, SINGLE NEEDLE TECHNIQUE

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### Background:

Optimal treatment for unicameral bone cysts remains unclear. Several treatments options evolved since the seventies of last century including; open curettage and grafting, steroid injection, bone marrow injection and finally demineralized bone matrix grafting.

This study evaluates the outcome of patients treated with percutaneous aspiration and injection with steroids and demineralized bone matrix.

### Materials and Methods:

Twenty four consecutive patients treated for UBCs since 1998 were eligible for inclusion; Median age was 10 year (range 4-41). Diagnosis was made radiographically, Seventeen patients received percutaneous treatment: Following aspiration with an 8 gauge bone needle, high pressure injection with contrast was performed, completely filling the cyst. After re-aspiration, depomedrol and demineralized bone matrix (DBX, Synthes, USA) were injected. While 7 patients underwent open curettage ,biopsy and grafting with DBX. Length of time to outcomes of complete/ incomplete healing or recurrence, were determined by radiographic analysis.

### Results:

Five patients who treated percutaneously recurred, and 2 who treated by open technique recurred; All 7 patients were treated percutaneously, two recurred and were treated with curettage and DBX grafting. Two patients (ages 4 and 6), recurred twice and healed after the 3rd treatment. Cyst location included 13 proximal humerus, 6 proximal femur, 4 calcaneus and one proximal fibula. 17 patients show new bone filling the cyst after a single treatment (median time of 2.5 months); 7 patients needed one or 2 more procedures to heal completely.

### Conclusion:

Demineralized bone matrix significantly improved healing following percutaneous treatment of UBC. Reossification was seen in most patients, unlike patients treated with steroid injection alone. This technique was simple and well tolerated and suggests that double needle and open techniques are unnecessary.

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## Progress in the Treatment of osteosarcoma.A Population-Based Study of 3089 Patients Diagnosed over 33 Years

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### Background:

The 1970s and 1980s saw great progress in the treatment of osteosarcoma, but subsequent trials have failed to improve the survival of patients with this disease.

### Methods:

We searched the Surveillance, Epidemiology and End Results (SEER) database for cases of osteosarcoma diagnosed between 1973 and 2005. Three eras were defined: era 1 (1973-1985), era 2 (1986-1995), and era 3 (1996-2005).

### Results:

We identified 3089 patients (median age, 19 years; 56% males) with osteosarcoma. Primary tumor sites were mainly the lower limbs (66%), upper limbs (11%), head and neck (8.8%), and pelvis (7.6%). Older patients had a higher proportion of axial tumors and a lower survival estimate. Survival improved significantly after 1986 ( $P < 0.0001$ ) but not after 1996 ( $P = 0.29$ ). A Cox proportional hazards regression model identified age, primary site, and stage as significant predictors of survival throughout the study period. Age  $> 45$  years at diagnosis, tumor sites other than head and neck and lower limbs, and metastatic tumors were significant adverse prognostic factors.

### Conclusion:

Despite early advances, more than a third of patients with osteosarcoma have continued to die for the past 2 decades. The worst outcomes occur in older patients, patients with primary tumors in unfavorable sites, and those with metastatic disease. There is an urgent need for more collaborative and basic research.

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## THE OUTCOME OF LIMB SALVAGE SURGERY IN A DEVELOPING COUNTRY, KHCC EXPERIENCE

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**Background:** Limb salvage surgery (LSS) became the standard surgical treatment for bone sarcomas since the late 1970s; however, LSS has high cost and numerous complications that make it less applicable in developing countries.

**Objectives:**

To Show that LSS in developing countries, can be compared to developed countries, when; team work, expert surgeon and enough resources are available.

**Methods:**

Since July 2006, a multidisciplinary team of sarcoma was established. This team consisted of pediatric and medical oncologists, radiation oncologists, radiologist, nurse coordinator and a full-time orthopedic oncology surgeon. The team was supported by a service for physical therapy. Clinical practice guidelines were established and a special protocol for rehabilitation following surgery was applied.

**Results:** Seventy patients with malignant or benign aggressive bone tumors presented at the study period, 5 patients received primary amputation, 65 patients received LSS (93% of all patients) included in our analysis, with mean follow up of 25 months (range, 6-53 months). Tumors were located in the extremities (n=59), in the scapula (n=3) and the pelvis (n=3). Histological diagnosis was: Osteosarcoma (n=29), Ewing's sarcoma (n=16), Chondrosarcoma (n=7), Giant Cell Tumor (n=5), Bone metastasis (n=5) and others (n=3). Endoprosthetic reconstruction used in 52 patients (47 modular, 3 expandable, 2 custom prosthesis), biological reconstruction in 7 patients, and no skeletal reconstruction in 6 patients. Local tumor control was achieved in 57 patients (88%). Among the complications encountered were: periprosthetic infection (n=5, 8%), traumatic dislocation (n=1, 1.6%), superficial skin necrosis (n=2, 3%), and radiation-induced stem loosening (n=1, 1.6%). Eight patients (12%) developed local recurrence. Limb survival was 95.4% at study end; three limbs had secondary amputation (one for local recurrence and 2 for persistent periprosthetic infection). All other types of complications were managed successfully. The average MSTS functional score for the 62 survived limbs was 87%.

**Conclusions:**

Our early results are encouraging. Patients with sarcoma are managed better within a multidisciplinary team that is familiar with highly specialized procedures including LSS. The early outcomes of our cases are comparable to that in developed countries in term of local control and prosthesis related complications.

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## FEMORAL HEAD DECOMPRESSION AND BONE GRAFT INJECTION USING NEW KIT

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### Background:

Avascular necrosis (AVN) of the femoral head is a pathologic process resulting from interruption of blood supply to bone. It can result from chemotherapeutic agents used for treatment of different cancer especially leukemia.

### Material and Methods:

16 patients and 21 Femoral head AVN, (Ficat stage I to early III) were treated using the Core decompression kit followed by injection with bone graft material Cortoss or Hydroset, 8 hips were stage III, 9 stage II and 4 stage I. All cases were done as day case surgeries with average operative time of 25 mins.

### Results:

16 hips had almost complete pain relief that persist at mean follow up of 3 years, 5 hips the pain persisted, all patients who had clinical response show radiological stabilization of the disease stage.

### Conclusion;

Femur head decompression using the Core decompression kit followed by bone substitute injection resulted in long term pain relief and prevention of AVN progression in 3/4 of patients. Core decompression when appropriately done, is safe, simple and effective way for pain relief and prevention of femur head AVN progression.

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## Shaped Graft for Aneurysmal Bone Cyst of Upper Limb Bones

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The optimal treatment of aneurysmal bone cyst remains challenging. We here present the results of using bone grafts shaped to the defects caused by aneurysmal bone cysts of upper limb bones. Fifteen patients (12 males & 3 females) with an average age of 12 years (range 6-16 years) were treated for aneurysmal bone cysts of upper limb bones by intra-lesional resection, argon beam coagulation and shaped bone graft. The grafts were harvested from 14 patients (11 fibulas & 3 iliac bones) and from the mother of one patient (proximal fibula). Osteosynthesis was required to stabilize the graft in four cases. The modified Enneking's scoring system was used for functional evaluation. One patient developed partial recurrence at 6 months and required reoperation. Superficial wound infection was encountered in one patient. Shortening of the humeral segment was seen in two patients (1 & 1.5 cm) but without angular deformity. After a mean follow-up of 43 months (range 20-64 months), the mean functional score was 97.3 %.

This technique is reliable to obtain a well reconstructed and growing bone with no or minimal deformity and good function.

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## Assection of neoadjuvant chemotherapy on volume surgical intervention in osteosarcoma of lower extremity

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**Background.** To estimate efficiency of neoadjuvant chemotherapy and its influence on volume of surgical intervention in osteosarcoma of lower extremity.

**Material and methods.** Treatment results of 122 patients with osteogenic sarcoma of tubular bones of lower extremity were studied. 34 patients (I group) are carried out system introduction antitumor preparations cyclophosphan 800 mg/m<sup>2</sup>, doxorubicin 60 mg/m<sup>2</sup>, cyplatin 100 mg/m<sup>2</sup>. 54 (II the group) - is carried out long intra arterial regional chemotherapy by scheme: doxorubicin 60 mg/m<sup>2</sup> 48 hours intra arterial (i/a) infusion, ciplatinin 100 mg/m<sup>2</sup> 6 hours (i/a) infusion and cyclophosphan 800 mg/m<sup>2</sup> (i/m). Long intra arterial regional chemotherapy under the similar scheme on the background of short-term hyperglycemia and local hyperthermia is carried out in 36 (III the group). Depending on efficiency from 1 to 4 courses of chemotherapy is carried out.

**Results.** 20 (58, 8 %) patients I group are made crippling operation (amputation or exarticulation), 14 (41, 2 %) - organ reserving operations (11-segmental resection with compression-destructed osteogenesis (CDO) by the device Ilizarev, 3-segmental resection of splint-bone). In II group, 30 patients (57, 7 %) are made crippling operations, 22 (42, 3 %) - reserved (10 -segmental resection with CDO, 7 - segmental resection of splint -bone, 5-segmental resection of bone with endoposthesis of the knee joint). In III group, 9 patients (25 %) are executed crippling operations, 27 (75 %) - preserving (20 - resection of bone with endoposthesis, 3-segmental resection with CDO, 4- segmental resection of splint- bone).

**Conclusion.** The application of long intra arterial chemotherapy on the background of local hyperthermia and short-term hyperglycemia increases the treatment efficiency of osteosarcoma of lower extremity bones and accordingly results in increase of quantity of organ reserving operations.

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## Selective arterial embolization of bone tumors

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**Background:** To assess the efficacy of selective arterial embolization for primary and metastatic bone tumors.

**Methods:** 18 patients with primary and metastatic bone were treated at RCRC RAMS in 2000-2011 years. Men - 10 (55.6%), women - 8 (44.4%). The average age  $47,28 \pm 14,42$  years, range 21-68 years. Primary lesion of bone - in 7 patients, metastatic - in 11 patients (mainly metastatic kidney cancer). Distribution by site of lesion: the spine - 12 cases, other departments - 6 cases. If it affects the spine, embolization was performed in corresponding segments (with the exception an Adamkiewicz artery). The goal of embolization: palliative care, sometimes in combined schemes - 10 cases, preoperative embolization of the arteries feeding the tumor to decrease intraoperative blood loss - 8 cases. Most often performed one embolization - in 16 patients, 2 patients - performed twice due to extensive network of collateral vessels. Used material: beads - in 10 cases (particle sizes ranged from 100 to 500), a spiral - in 8 cases.

**Results:** In 100% of cases, embolization was technically successful. In 6 (33.3%) cases a residual blood remained within 5-30%. Clinical response after palliative embolization obtained in 90% of cases in the form of pain relief, improvement of limb function. In 75% of cases of preoperative embolization it was possible to achieve significant decrease intraoperative bleeding during subsequent operation. Postembolization syndrome was present in most patients, paresthesias were observed in 27.8% of cases. Severe complications of embolization was not noted.

**Conclusion:** Selective embolization of the arteries - the impact of an effective option in the treatment of primary and metastatic bone tumors for palliation or as part of combination therapy, as well as preoperative treatment for reducing the risk of surgery and blood loss. Careful feeding artery embolization, especially if you have many collaterals, is necessary to achieve an adequate effect.

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## Indication to the osteosynthesis associated with curettage in benign and malignant bone tumors

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**INTRODUCTION:** The bone cavity remaining after the curettage of the neoplastic lesion often requires the use of filling systems able to ensure mechanical stability to the system. The literature analysis shows that the routine filling of curetted bone lesions does not appear to be necessary from a mechanical point of view and no biomechanical testing has been done to assess fixation techniques in pathological fractures.

**OBJECTIVES:** Evaluate according to the size of the bone defect, the region of the injury, the need to use with acrylic cement and bone substitutes an additional systems such as osteosynthesis to guarantee a mechanical stability of the bone.

**METHODS:** We analyzed twenty bone lesions localized in femur or humerus treated with curettage associated to the osteosynthesis

**RESULTS:** The malignant lesions were treated with extended curettage with use of high speed cutters and liquid nitrogen filled with acrylic cement while the benign lesions were treated with curettage filled with synthetic bone or acrylic cement associated with osteosynthesis with plate and locked screws. The analysis showed no recurrence of the lesion, no infection, two cases of stiffness of the knee. Three patients treated with only curettage had a fracture and therefore they underwent to osteosynthesis with plate.

**CONCLUSION:** The curettage with bone grafting or bone replacement or cement is not always recommended in the treatment of bone tumors. The loss of bone mass after curettage requires to fill this lesion to give stability to the bone.

There are no data in the literature that demonstrate the extent of the size of a lesion that require the osteosynthesis. PMMA is recommended in benign aggressive and malignant lesions of low grade. In our opinion, the filling is essential in the large lesion to ensure a mechanical support. In our opinion an adequate exposure and an accurate curettage is essential but required an osteosynthesis in large lesions (> 5 cm), in lesions localized in distal femur, in lesion in loading areas, in obese patients, in case of use of adjuvants local, in case of a very large windows bone to do the curettage and if the patient needs of an high functional requirements

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## Tumor reconstructive surgery using recycled autobone Anticipating the complications

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**Background:** Joint-saving surgery is the current trend in musculoskeletal tumor surgery. A very important method is reconstruction using recycled autobone. It is readily accessible, facilitating easy reconstruction due to its size and shape specific to the host bone defect and is acceptable in many developing countries with very delicate social and religious beliefs

**Purpose:** The aim of this study is to evaluate the outcome of reconstructive surgery using either pasteurized or irradiated autograft bone and presenting the possible complications.

**Patients and Methods:** Sixteen patients of Kyungpook national university hospital over the period of 1995-2010 who had undergone tumor resection and bone reconstruction using pasteurization or irradiation method and a minimum of 2 years follow-up were retrospectively reviewed.

**Results:** Our graft survival rate is 83.3% and infection rate is 6.3%. There were no local tumor recurrence and graft nonunion in this series. Five patients developed limb length complications necessitating additional surgical procedures.

**Conclusion:** Our experience is similar to the other reports on reconstructive surgery using recycled autobone. Effective delivery of neoadjuvant chemotherapy, better intraoperative imaging, and the surgeon's surgical skills and mastery of the concepts in both musculoskeletal surgery and osteosynthesis are prerequisite for a successful surgery. Anticipating the potential complications is also very important to maximize the patient's benefits in such procedure.

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## Long-term results of endoprosthesis replacement of large joints in patients with bone tumors

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**Background:** We evaluated the long-term clinical results and the survival of the prostheses of patients who had a limb-sparing procedure by means of the implantation of a large-segment prosthesis. Function was evaluated with the revised 30-point classification system of the Musculoskeletal Tumor Society. The survival of the prostheses was analyzed with regard to several variables with use of Kaplan-Meier survival estimates.

**Methods:** During the period from 1979 to 2010 year in RCRC 1181 primary operations performed in the volume of replacement of large joints of various locations, among the interventions were resected bones forming the shoulder (n = 134), elbow (n = 10), hip (n = 167), knee (n = 786), and ankle joints (n = 8). Endoprosthesis with total hip replacement n = 50, humerus, n = 16, tibia n = 1. The defect is replaced by the individual and modular endoprosthesis. The defeat of the bones were due to primary tumors in 92% of patients, metastatic - 8%. The average age of patients was 28 ± 14 years (from 10 to 80 years), 53.5% were men, women - 46.5%. Osteosarcoma predominated (46%) in the remaining cases were diagnosed chondrosarcoma (10%), Ewing's sarcoma (5%), giant cell tumor (14%), other morphological forms consisted of 25%.

**Results and Conclusion:** The average follow-up was 10 years old. Overall survival is 61%. The recurrence rate was 12%. Among the complications of infection are marked (11%), instability of the prosthesis (13.7%). The prosthesis survival corresponded to 54%. Functional evaluation of MSTS score was 70% for operations on the shoulder joint endoprosthesis, 80% - for the hip. MSTS after arthroplasty of the femur consistent 58% - with its total replacement and 92% - of the distal resection, evaluation after resection of the proximal tibia - 75% and 72% at the distal.

**Conclusion:** Endoprosthetic reconstruction gave satisfying functional and oncological results and low rate of complications in most patients after long-term survival. Limb salvage surgery is the gold standard of modern onco-orthopedics

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## Minimal invasive surgery for unicameral bone cyst using demineralized bone matrix: a case series

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**Background:** Various treatments for unicameral bone cyst have been proposed. Recent concern focuses on the effectiveness of closed methods. This study evaluated the effectiveness of demineralized bone matrix as a graft material after intramedullary decompression for the treatment of unicameral bone cysts.

**Methods:** Between October 2008 and June 2010, twenty-five patients with a unicameral bone cyst were treated with intramedullary decompression followed by grafting of demineralized bone matrix. There were 21 males and 4 female patients with mean age of 11.1 years (range, 3–19 years). The proximal metaphysis of the humerus was affected in 12 patients, the proximal femur in five, the calcaneum in three, the distal femur in two, the tibia in two, and the radius in one. There were 17 active cysts and 8 latent cysts. Radiologic change was evaluated according to a modified Neer classification. Time to healing was defined as the period required achieving cortical thickening on the anteroposterior and lateral plain radiographs, as well as consolidation of the cyst. The patients were followed up for mean period of 23.9 months (range, 15–36 months).

**Results:** Nineteen of 25 cysts had completely consolidated after a single procedure. The mean time to healing was 6.6 months (range, 3–12 months). Four had incomplete healing radiographically but had no clinical symptom with enough cortical thickness to prevent fracture. None of these four cysts needed a second intervention until the last follow-up. Two of 25 patients required a second intervention because of cyst recurrence. All of the two had a radiographical healing of cyst after mean of 10 additional months of follow-up.

**Conclusions:** A minimal invasive technique including the injection of DBM could serve as an excellent treatment method for unicameral bone cysts.

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## Soft Tissue Sarcoma Abutting The Bone, What Surgery Is The Most Appropriate?

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### Back ground:

The incidence, surgical treatment and effect on overall survival and recurrence of bone invading/abutting soft tissue sarcoma, still poorly described in the literature.

### Objectives:

To present an institutional experience regarding; surgical treatment and outcome of soft tissue sarcoma abuts the bone.

### Material and Methods:

From July 2006 till Dec. 2010, 55 patients with STS treated with Limb Salvage Surgery (LSS), at King Hussein Cancer Center. Seventeen patients (31%) the tumor were abutting the bone, 15 patients as first presentation and 2 as recurrent disease, age 15-65 year, Median age 49 years.

Tumor location includes: thigh (n=8), arm (n=2), forearm (n=2), leg (n=3), low back and chest wall one patient each. Synovial Sarcoma was the commonest histological diagnosis (n=6), 12/17 patients received bone surface burring after resection of the mass with the periosteum and 10 of them followed by post operative radiation therapy; 5/17 patients in whom signs of cortical invasion and early destruction seen in MRI, we resect the adjacent cortex en-bloc with the tumor, none of them received adjuvant radiation.

### Results:

At mean follow up of 30 months, (10-58), 4 patients died due to metastatic disease, 2 patient developed metastatic disease and still on palliative care, and 2 patients developed local recurrence (12%), one with leg disease received en-bloc resection of the cortex and other with per sacral tumor received bone surface burring). One patient developed radiation related femur fracture. 3 years event free survival was 53% and overall survival 76%.

### Conclusion:

This is a retrospective pilot study with small group; the results show that STS abutting bone probably do not lead to worse outcome, bone surface burring or uni-cortical resection is sufficient, and maybe there is no need to do bi-cortical bone resection. Multicenter cooperation is needed to recruit more patients to have statistically significant number.

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## Clinical outcome following marginal resection of atypical lipomatous tumor/well-differentiated liposarcoma of the extremities and trunk wall

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**Background:** The consensus of the best surgical procedure for atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDLS) still remained unclear. The wide resection may cause a serious functional disorder, otherwise the marginal resection may increase the risk of local recurrence. This study describes our experience with this tumor of the extremities and trunk wall when treated by marginal resection. **Methods:** We retrospectively reviewed 40 ALT/WDLS patients treated by a marginal resection between 1997 and 2011. There were 20 men and 20 women, with an average age of 60.1 years. The average size of the tumor was 15.4cm. The most common site was the lower extremities (24 patients), followed by the trunk (10 patients), and upper extremities (6 patients). Intermuscular tumors were founded in 21 patients, intramuscular tumors in 16 patients, and subcutaneous tumors in 3 patients. The mean follow-up duration was 4.7 years. **Results:** Three patients (7.5%) had a local recurrence at an average of 6.8 years after initial resection. One of these tumors was founded in the lower limb and two in the trunk. Two patients had local recurrences more than two times. The first CT scan or MRI at 4 months after initial surgery revealed residual tumor in other three patients (7.5%) after initial surgery. All of these tumors were intermuscular. Serious functional loss did not occur in all patient of this series. There was no case of metastasis or dedifferentiation. **Conclusion:** Our findings suggested that a marginal resection for ALT/WDLS of extremities and trunk wall seem to be adequate treatment as they have a slight tendency to recur but do not metastasize; however, long-term follow-up is recommended for early diagnosis and treatment of any local recurrence. In case of intermucular tumor, a careful excision may reduce the risk of leaving tumor.

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## The use of neo-adjuvant radiotherapy in the management of peri-articular soft tissue sarcoma

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**Background:** Optimising post-operative joint function is challenging when treating peri-articular soft tissue sarcoma. Radiotherapy minimises local recurrence rates in management of soft tissue sarcoma. Differences in risks and benefits depend on adjuvant or neo-adjuvant use. The lower doses and smaller treatment volumes achieved with pre-operative radiotherapy have potential benefits for the management of peri-articular sarcomas. This study therefore aims to assess short-term outcome measures and complications after treatment with neo-adjuvant radiotherapy and surgery for patients with soft tissue sarcoma

**Patients and Methods:** 17 patients with soft tissue sarcoma were identified as being treated with pre-operative radiotherapy. 3D conformal radiotherapy was delivered at a single centre with a dose of 50Gy in 25 fractions over 5 weeks. Patients were assessed weekly for adverse effects. Resection was planned 4-6 weeks after radiotherapy.

**Results:** Medial follow-up was 13 months (range 5-44 months). No patients had significant adverse effects during radiotherapy. One patient had surgery delayed due to local reaction. Histology demonstrated 50-100% tumour necrosis in all tumours except one patient with pleomorphic liposarcoma, showing no detectable necrosis. Major complications occurred in one patient (persistent foot drop) and six patients had minor complications (three superficial infections, two seromas, one transient neuropraxia). One patient required further surgery due to incomplete margins. TESS scores for upper and lower limb patients were 86.1 and 78.1 respectively. No local recurrences to date have been recorded. One patient developed metastatic lymphadenopathy and another has developed lung metastases.

**Conclusions:** This work has demonstrated that major complications are minimal and early function and local control rates are excellent. Long term follow-up is required to demonstrate final functional outcome and local control rates.

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## Early results of the treatment of lower limb myxoid liposarcoma using neo-adjuvant or adjuvant radiotherapy at a single centre

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**Background:** Liposarcoma accounts for approximately 17% of all soft tissue sarcomas, with 45-55% being diagnosed as the myxoid variant. Neo-adjuvant radiotherapy has potential benefits to adjuvant radiotherapy in soft tissue sarcoma management due to lower dosage and reduced treatment volume, but has a theoretical increased risk of wound healing complications. We have adopted neo-adjuvant radiotherapy as a standard treatment in the management of myxoid liposarcoma, with the initial results being compared to patients treated with conventional post-operative radiotherapy.

**Patients and Methods:** 14 patients who received operative intervention for a diagnosis of myxoid liposarcoma between June 2006 – June 2012 were identified, with six receiving neo-adjuvant radiotherapy and eight receiving adjuvant radiotherapy. Mean follow-up was 21 months (range 5-75 months).

**Results:** Patients treated with neo-adjuvant radiotherapy demonstrated a reduction in largest tumour dimension from 93.8mm to 69.4mm on MRI scan, and all had negative margins on resection. Two of the eight patients treated conventionally with surgery had positive resection margins, with negative margins obtained after further resection prior to radiotherapy. The neo-adjuvant group had one major complication (persistent foot drop) and three minor complications (two seromas and one wound infection). The adjuvant group showed two major complications (persistent post-operative pain) and one minor complication (wound infection). TESS scores were similar between neo-adjuvant and adjuvant patients (80.6 vs 78.5).

**Conclusions:** Initial results suggest that neo-adjuvant radiotherapy may confer benefits over adjuvant radiotherapy without adversely affecting complication rate. A larger sample size and longer follow-up will identify if the benefits demonstrated in this study are significant with comparable local control rates.

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## **Management of Myxofibrosarcoma in a Single Specialist Centre**

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**Background:** Although soft tissue sarcoma is a rare malignancy, myxofibrosarcoma is a common form diagnosed. Myxofibrosarcoma is complicated by a high local recurrence rate (18-54%) and significant morbidity following treatment, hence management can be challenging.

**Patients and Methods:** Patients treated between 2003 – 2012 were identified via a database within the histopathology department and case notes were retrospectively assessed. All histology samples were reviewed by a senior histopathologist to ensure a correct diagnosis.

**Results:** 29 patients (12 male, 17 female) with an average age of 61 years (range 19-89 years) underwent surgery at a single centre, with 24 patients receiving adjuvant and two receiving neo-adjuvant radiotherapy. 22 patients had lower limb and 7 had upper limb tumours. 3 were treated for secondary recurrence after having primary surgery elsewhere. 21 patients had Trojani Grade 2 or 3 tumours. All underwent limb-sparing surgery initially but six patients (20.7%) suffered local recurrence after an average follow-up of 28 months and all ultimately required above knee amputation. Four patients developed wound infection, with one requiring VAC therapy. One patient required a flap repair of the forearm. 5-year survival rate was 87.5%.

**Conclusions:** Our results compare favourably against results published so far in the literature with a low local recurrence rate and mortality. Limb-sparing surgery aims to reduce morbidity and disability following treatment but more research is required in adjuvant treatments to further reduce the risk of local recurrence of tumour.

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## FUNCTIONAL RESULTS AND QUALITY OF LIFE AFTER OPEN SYNOVECTOMY FOR GIANT CELL TUMORS OF SYNOVIUM IN THE KNEE

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**BACKGROUND** Diffuse-type giant cell tumors(Dt-GCT) are benign but locally aggressive synovial lesions. Although arthroscopic synovectomy(AS) is advocated as alternative to open synovectomy(OS) to minimise surgical morbidity, recurrence-rates after AS remain unacceptably high. Our study aim was to evaluate the influence of (multiple) synovectomies on functional outcome and quality of life(QOL) of patients with Dt-GCT in the knee treated in a tertiary center(1980-2010).

**METHODS** We retrospectively reviewed 36 patients, eight were excluded with <1.5 year follow-up and 8 without functional and QOL data. Twenty patients were included: 12 referred with recurrence and eight primarily treated at our center. Median follow-up was 7.7years (1.6-15.9). Eleven patients were male. Mean age at final follow-up was 45.9years (11-77). We evaluated recurrence rates, Knee-injury and Osteoarthritis-Outcome-Score(KOOS), Musculoskeletal Tumor Society(MSTS), Toronto Extremity Salvage Score(TESS) and Short Form(SF)-36.

**RESULTS** Eleven patients underwent AS and one OS before referral to our center, where OS was performed for recurrent Dt-GCT. Five of these 12 patients developed further recurrences (42%) and were treated with repeated OS. Three of the referred patients had severe recurrent disease and finally underwent distal femur resection and prosthetic reconstruction (one revision surgery for prosthetic loosening). Eight other patients underwent primary OS in our hospital; two developed local recurrence (25%), one treated with repeated OS and one with AS. No severe complications were noted in this group (one urinary tract infection and one haemarthros).

Overall, patients primarily treated at our center with OS with no subsequent recurrence had higher mean KOOS, MSTS, TESS and SF-36, after mean 6.6years follow-up (Figure 1). Multiple synovectomies resulted in significant lower KOOS-Pain ( $p=0.024$ ), KOOS-Symptoms ( $p=0.041$ ), KOOS-QOL ( $p=0.032$ ) and TESS ( $p=0.016$ ), after mean 7.1years follow-up.

**CONCLUSION** As the majority of patients were referred to our center with recurrent disease, we had the opportunity to evaluate the influence of (multiple) synovectomies on functional outcome and QOL. After primary OS, recurrence rate was acceptable and functional outcome and QOL were good. Functional and QOL-scores were significantly lower in patients with multiple synovectomies. In our opinion, centralized primary radical OS is advocated, in order to decrease local recurrence-rates and improve postoperative functional outcome and QOL.

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## Surgical management of soft tissue sarcoma with reconstruction in patients aged over 80 years

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### Background

The use of a local rotational flap as well as a free vascularized flap may be necessary for closure of large defects after resection of primary soft tissue sarcomas (STSs). However, it is often difficult to offer these procedures for markedly aged patients because of the generalized concept that such patients have low tolerance for them. The aim of this study was to evaluate the oncological and functional outcomes of flaps in patients over 80 years of age with STSs.

### Methods

From our database (since 1998) of all patients with STSs, those aged over 80 years who underwent surgical resection with reconstructive procedures were identified and reviewed.

### Results

Six patients (3 males and 3 females) were treated for STSs with reconstructive surgery after primary resection. Median age at presentation was 84 years. The average tumor size was 7.9 cm. The site of the tumor was the lower leg in 2 patients, chest wall in 2, and back and buttock one patient each. Three patients were diagnosed as having undifferentiated pleomorphic sarcoma (all high grade) and the others were diagnosed as having myxofibrosarcoma (1 low grade and 2 high grade). The tumor stage was IIB in 2 patients, III in 2, IB in 1, and IIA in 1. Three patients underwent wide surgical resection with a free latissimus dorsi (LD) flap, and in the others a local rotational flap was used (2 LDs and 1 rectus abdominis). Although one of the patients with a local rotational LD flap suffered wound infection as a postoperative complication, the flap was a success in 5 patients. No patients suffered local recurrence, while 3 patients developed distant metastases during their clinical course. The median follow-up period was 20 months (range, 3-43 months). Among the 6 patients, 3 were CDF, 2 were AWD and 1 was NED.

### Conclusions

Flap outcome in patients aged over 80 years was comparable with that in younger patients. The present findings suggest that even extremely aged patients (over 80 years old) can tolerate not only rotational but also free flap reconstruction well with low rates of acceptable postoperative complications.

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## Atypical Lipomatous Tumour /Well Differentiated Liposarcoma: A Plea for Clarity

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### Background:

Atypical Lipomatous Tumour /Well Differentiated Liposarcoma (ALT/WDL) is a common tumour with very low metastatic potential. However, the terminology, diagnosis and treatment of patients with ALT/WDL are currently not standardised. The aim of this study was firstly to collate data on the management of ALT/WDL; and secondly to utilise this data to produce a consensus statement for the management of ALT/WDL.

### Methods:

A 15-question online survey was sent worldwide mainly to oncologists, pathologists and orthopaedic oncology surgeons. Questions were designed to target ambiguous areas of the diagnosis and management of ALT/WDL.

### Results:

Survey responses were received from many centers around the world. With regards to initial investigation(s) for ALT/WDL, 36.8% undertake MRI in all patients, regardless of tumour size/anatomical location, whilst a further 36.8% use MRI in patients with a suspected tumour size  $\geq 5$ cm, and 7.0% with a suspected size  $\geq 10$ cm. In addition, 45.3% of respondent's biopsy suspected ALT/WDL prior to resection, whilst 54.7% do not. Interestingly, 26.2% of respondents perform a wide local excision for ALT/WDL, whilst 73.8% undertake marginal resections. 45% of the respondents would organize a staging CT scan of chest and 42% would obtain follow up chest radiographs despite the fact that more than 95% have never come across metastases from ALT/WDL.

### Conclusions:

As anticipated, this survey indicates that the current clinical management of ALT/WDL is extremely variable. It is suggested that a consistent nomenclature would facilitate the appropriate management of ALT/WDL. In addition, a consensus document based on the survey data for ALT/WDL is proposed.

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## **Nodular fasciitis: clinical characteristics and natural course**

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### **INTRODUCTION**

Nodular fasciitis is a benign tumefaction of myofibroblasts. Because of similarity of clinical presentation with sarcoma, it is also called as pseudosarcoma fasciitis and pseudosarcoma fibromatosis. The concern about possibility of a sarcoma leads to surgical excision as a mainstay of treatment.

Therefore, understanding of clinical characteristics and course can prevent a clinician from performing unnecessary procedures including surgical excision or even biopsy for this small and self-limiting lesion.

In this retrospective review, we asked 1) demographic findings 2) clinical characteristics and 3) natural course of nodular fasciitis.

### **METHODS**

This study included thirty-one patients who were pathologically confirmed with nodular fasciitis between January 2008 and June 2012. There were 14 males and 17 female patients with mean age of 34.5 years (range, 9-57years). Eleven lesions were located in the forearm, seven in the upper arm, five in the thigh, four in the lower leg, two in the neck area and two in the hand. The mean size of the lesion at the initial visit was 1.5cm (range, 0.5-4.5cm). Seventeen patients had memory of pain on the lesion during the initial presentation. The duration of symptom ranged from 3 days to 1 month.

### **RESULTS**

Nineteen lesions were surgically removed. None of them recurred at the last follow-up. Twelve patients were periodically followed-up after confirmation of nodular fasciitis by core needle biopsy. Ten of the 12 lesions were spontaneously resolved. The time interval between diagnosis and resolution ranged from 1 month to 7 months. In the other two, the lesions were involuting but still remained until 8 and 9 months follow-up.

### **CONCLUSIONS**

Characteristic clinical findings are important to confirm the diagnosis of nodular fasciitis. Most of nodular fasciitis spontaneously resolved. After ruling out a sarcoma by clinical suspicion or core needle biopsy, periodical observation would be recommendable for this self-limiting lesion.

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## Ray of light -Neo-adjuvant chemotherapy for primary high-grade extremity soft tissue sarcoma

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**Background:**The aim of this study was to retrospectively analyze the relationship between neo-adjuvant chemotherapy and outcome in patients with high-grade extremity soft tissue sarcomas (STS).  
**Patients and methods:** Inclusion criteria were high-grade, deep, >5 cm extremity soft tissue sarcomas. Twelve patients (seven male and five female patients) diagnosed between 2006 and 2012 were. Median age was 51 years (21 to 67 years). Three patients had malignant fibrous histiocytoma, four patients had MPNST, two patients had rhabdomyosarcoma, one patient had liposarcoma, one had myxofibrosarcoma and one had malignant mesenchymoma. All patients were treated with three cycles of neoadjuvant chemotherapy. Patients with malignant fibrous histiocytoma were treated with doxorubicin/cisplatin/metotrexate and patients with all other STS were treated with doxorubicin/ifosfamide/mesna. After neoadjuvant therapy all patients with control of disease were treated with surgery and adjuvant chemotherapy.

**Results:** Response rate was 42% (five patients achieved partial response) registered according to RECIST criteria. Control of disease (partial response, minor response and stable disease) was 83%. Two patients (17%) experienced progression of disease during therapy with local progression of disease. Limb sparing surgery was performed at ten patients (83%). Overall survival was 33 months (range 6 to 79 months, 95% CI) with nine patients still alive, seven without progression of disease.  
**Conclusion:** Our result suggests that neoadjuvant chemotherapy is an effective regimen in treatment of advanced STS. These data emphasize the need for further prospective clinical studies of neo-adjuvant or adjuvant chemotherapy for patients with large high-grade extremity sarcomas.

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