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Non-metastatic osteosarcoma of the extremity. Neoadjuvant chemotherapy with methotrexate, cisplatin, doxorubicin and ifosfamide. An Italian Sarcoma Group survey.

Stefano Ferrari¹, Cristina Meazza², Franca Fagioli³, Angela Tamburini⁴, Raffaele Cozza⁵, Virginia Ferraresi⁶, Maurizio Mascarin⁷, Gianni Bisogno⁸, Piero Picci⁹

¹) Istituto Ortopedico Rizzoli ²) INT, Milano ³) OIRM, Torino ⁴) Meyer, Firenze ⁵) OPBG, Roma ⁶) IFO, Roma ⁷) CRO, Aviano ⁸) Ped. Oncol., Padova ⁹) IOR, Bologna, Italy

Background: According to the results of the ISG/OS-1 study (April 2001-December 2006), the neoadjuvant regimen MAP (Methotrexate (MTX), doxorubicin (ADM), cisplatin (CDP), and ifosfamide (IFO) postoperatively added in poor responder patients, was recommended for patients with non metastatic osteosarcoma of the extremity treated in the ISG centers.

Patients and Methods: The data of patients with non metastatic osteosarcoma of the extremity, aged ≤ 40 years, treated in the ISG centers, were prospectively collected in the ISG WEBSITE database.

Compared to ISG/OS-1 (cumulative doses: ADM 420mg/m², MTX 120g/m², CDP 600 mg/m², IFO 30g/m²) the recommended regimen foresaw a reduction of the courses of MTX from 10 to 5 for a cumulative MTX dose of 60g/m².

Results: From January 2007 to June 2011, TOT patients (median age was 16 years (from 4 to 40), male TOT%) were registered. TOT (%) patients underwent limb-salvage surgery. Chemotherapy-induced necrosis was good (≥90%) in 48% of patients. No treatment-related deaths were recorded. With a median follow-up of 39 months (4-80), 5-year OS was 80 % (95% CI, 73 to 87%) and EFS was 50% (95% CI, 39 to 59%). In ISG/OS-1 the rate of limb salvage and good histological response were 92% and 48% respectively. 5-year OS was 73% (95% CI, 65-81%) and EFS was 64% (95% CI, 56-73%).

Conclusions: While the response rate and the limb salvage rate recorded in the survey are in the same range of the previous study, the percentage of EFS is lower than that expected. This difference might be due to the observational characteristics of the survey, but we cannot exclude a possible role played by the reduction of the cumulative dose of MTX.

E-mail (main author): stefano.ferrari@ior.it



O1:102

Current indications for cryosurgery in orthopaedic oncology

Domenico Andrea Campanacci¹, Guido Scoccianti¹, Francesca Totti¹, Filippo Frenos¹, Serena Puccini¹, Giovanni Beltrami¹, Rodolfo Capanna¹

¹Azienda Ospedaliera Universitaria Careggi, Italy

Background:

Local adjuvant treatment in aggressive benign or low grade malignant bone tumors is the traditional application of cryosurgery in orthopaedic oncology. Introduction of new cryosurgical devices using probes to deliver cryotreatment has made the technique safer in comparison to liquid nitrogen and is allowing new and expanding indications.

Methods:

Since 2000 we have used cryosurgery in 42 surgical procedures with the following indications:

A - Local adjuvant treatment in (A1) aggressive benign and low grade malignant bone tumors or metastases after intralesional surgery in selected high risk lesions (wide dimensions, iuxtarticular localization). An extended application can be sterilization of margins after at risk wide excision in high grade tumors (A2). A1 (15 patients): GCT 7, epithelioid haemangioma 3, low grade chondrosarcoma 2, chondroblastoma 1, ABC 1, renal carcinoma metastasis 1. A2 (1 patient): osteosarcoma sacroiliac region 1.

B - Bleeding control (B1) and/or solidification of mucoid/myxoid tumors (B2) + adjuvant treatment during curettage in at risk anatomical sites like pelvic or shoulder girdle. B1 (20 patients): renal or thyroid carcinoma metastasis 7, GCT 4, ABC 2, metastatic hemangiopericytoma or hemangioendothelioma 2, schwannoma 1, chordoma 1, angioma 1, chondrosarcoma 1, myeloma 1. B2 (1 patient): giant myxoid chondrosarcoma 1.

C - Post-excisional sterilization (liquid nitrogen immersion) of bone segments for reconstruction by massive autologous bone grafting. 3 patients: synovial sarcoma 2, chondrosarcoma 1.

D - Percutaneous treatment of metastases or inoperable recurrent primary bone tumors. 2 patients: metastatic chordoma 1, recurrent Ewing sarcoma 1.

Results:

No neurological or vascular damages occurred. At follow up ranging from 12 to 144 months, one deep and one superficial infection were observed. One patient developed superficial skin necrosis. In group A and B1, two recurrences occurred (GCT 1, ABC 1) in 21 patients with a follow-up longer than 12 months. No fractures of on-site treated segments were observed, may be due to a frequent use of preventive plate fixation. One fracture of a cryotreated autologous bone graft was observed.

Conclusion: Our series confirms safety and efficacy of cryosurgery and supports its application in a growing number of new indications in orthopaedic oncology.

E-mail (main author): campanaccid@gmail.com



O1:103

Exploring Multiferon Therapy in Patients with Desmoid Tumours in need of Medical Treatment where Surgery is not a Feacible Option.

Jan Peter Poulsen¹, Olga Zaikova¹, Annette Skeie¹, Bodil Bjerkehagen¹, Jan Magnus Poulsen¹, Kirsten Sundby Hall¹

¹Oslo University Hospital, Norway

Background:

Desmoid tumours (aggressive fibromatosis) are locally invasive, non metastatic, but have a high local recurrence rate after primary resection. The tumours can occur in all ages, but the majority of patients are women, often of childbearing age. In patients, where surgery is not an option, medical treatments may be needed. Because positive responses with INF- α therapy had been reported, supported by in-vitro and in-vivo results, we decided to investigate Multiferon as a treatment option for patients with these tumours.

Methods:

Multiferon is a multi subtype INF- α product obtained from the leukocyte fraction of human blood. The product is highly purified and contains α 1, α 2, α 8, α 10, α 14 and α 21. Multiferon was given sc 3 Mill IE x 6/week as a standard, but with some variations in compliance. Included were inoperable patients with progression of disease needing therapy and not candidates for RT, chemotherapy or hormone therapy for different reasons

Results:

From January 2008 to January 2013, 22 pts have been evaluated for starting Multiferon treatment, 14 women and 8 men. Of these 22pts, 4 have not yet received Multiferon. 4 pts are still on treatment. 5 pts achieved PR, 11 pts SD, 1 pt PD and 1 pt not evaluated yet. None of the pts have progressed after end of treatment. Pts have been treated from 2 -38 months. and have been observed from 0 to 30 months after ending treatment. Treatment was stopped when the pts wanted to, either due to side effects or achieving stable disease observed over several months. Side effects were as expected with Multiferon, generally tolerable, manageable and reversible. All pts were happy ending the treatment.

Conclusions:

Multiferon may be a new promising treatment option for desmoid tumours. More data are needed. The presentation will present latest new follow-up data.

E-mail (main author): jpp@ous-hf.no



01:104

Isolated Limb Perfusion – Experience at the West German Cancer Center

Georg Täger, Hans Ulrich Steinau, Lars Eric Podleska

West German Cancer Center Essen, Germany

Background:

Isolated limb perfusion (ILP) is based on the local application of recombinant TNF- α and melphalan (TM-ILP) and reported to represent one of the most effective local treatment modalities for soft tissue sarcoma (STS) of the limbs. On various papers TM-ILP has been reported to result in excellent local response rates, ranging from 45% up to more than 80% for partial and complete remissions. Hence limb salvage has become more than a realistic purpose even in those patients whose limbs were at risk by advanced and non resectable soft tissue sarcoma.

Methods:

This paper reports on TM-ILP at a tertiary cancer center reflecting more than ten years and roughly 300 procedures performed for soft tissue sarcoma. Beside the enormous response rates and limb salvage rates which are in line to the reports of other centers, the following aspects are highlighted.

Results:

Assessment of clinical response using size based WHO-criteria as well as RECIST has been shown to be insufficient as none of those criteria were able to reliably identify the extent of regression after TM-ILP. Subtypes of STS do only differ little regarding the characteristics of regression with fibrosis/sclerosis being the most upon histopathology. Interestingly, when evaluating micro-vessel density (MVD), vascularisation of STS did not significantly impact on regression despite of the fact that TNF- α does target tumor's blood supply. Undoubtedly, TM-ILP does improve the integrity of the tumor surrounding capsule as well as the width of surrounding fibrous tissue. That explains why such a high rate of regression and local control could be achieved even in marginally resected STS which were judged as non resectable prior to TM-ILP.

Conclusion:

Based on this experience, it has become clear that TM-ILP should be provided for those patients where limb salvage or preservation of limb function cannot be achieved by surgery and radiotherapy alone. More precisely, TM-ILP should be an integral part of treatment modalities in all tertiary cancer centers. The histopathologic reflection of subgroups intends to extend the indication on all those patients with advanced STS where pretreatment might reduce the extent of loss of function by effectively sparing soft-tissues and neurovascular structures.

E-mail (main author): georg.taeger@uk-essen.de



O1:105

Isolated limb perfusion for primary, locally advanced soft tissue sarcomas of the extremities - prognostic factors and outcome

Dimosthenis Andreou¹, Mathias Werner², Bjoern Jobke³, Henrike Boldt³, Frank Traub³, Daniel Pink⁴, Peter Reichardt³, Per-Ulf Tunn³

¹) University Hospital Muenster ²) HELIOS Klinikum Emil von Behring, Berlin ³) HELIOS Klinikum Berlin-Buch ⁴) HELIOS Klinikum Bad Saarow, Germany

Background: Isolating limb perfusion (ILP) with TNF α and melphalan is an effective neoadjuvant modality for locally advanced, extremity soft tissue sarcoma. The objective of this study was to evaluate the oncological outcome and identify possible prognostic factors.

Methods: The files of 63 patients with primary, locally advanced, non-metastatic extremity soft tissue sarcoma, who underwent neoadjuvant ILP followed by delayed surgical resection at our department between 2001 and 2011, were retrospectively analyzed. Mean follow-up amounted to 49 months (range, 8-138 months) for all patients and 58 months (range, 12-138 months) for survivors.

Student's t-test was used to compare means. Survival curves were calculated with the Kaplan-Meier method and compared with the log-rank test. **Results:** Mean tumor size prior to ILP was 10 cm (range, 3-34 cm), compared to 9 cm (range, 0-33 cm) after ILP ($p=0.015$). 23 patients had a good histological response, according to the Salzer-Kuntschik criteria. The mean mitotic rate prior to ILP amounted to 33 mitoses/10 high-power fields (HPF), compared to 15 mitoses/10 HPF after ILP ($p=0.077$). 32 patients underwent a PET or PET-CT prior to and 6 weeks following ILP. The mean SUVmax prior to ILP was significantly higher than after ILP (11.4 vs. 6.9, $p=0.001$).

Overall and metastasis-free survival at 5 years amounted to 62% and 56%, respectively. Histological response according to the Salzer-Kuntschik criteria, SUVmax prior to ILP and the mitotic rate prior to ILP did not correlate with overall or metastasis-free survival. However, a low mitotic rate after ILP, a low SUVmax after ILP, and a small tumor size both before and after ILP were all significantly associated with an improved overall ($p=0.033$, $p=0.006$, $p=0.015$ and $p=0.015$, respectively) and metastasis-free survival ($p=0.018$, $p=0.005$, $p=0.004$ and $p=0.002$) respectively.

Conclusion: Tumor size both before and after ILP, SUVmax following ILP and the mitotic rate in the surgical specimen could be identified as significant prognostic factors for patients with locally advanced extremity soft tissue sarcomas undergoing neoadjuvant ILP with TNF α and melphalan.

E-mail (main author): dimosthenis.andreou@ukmuenster.de



O1:106

The value of isolated limb perfusion in the treatment of differently graded liposarcomas

Lars Erik Podleska¹, Benjamin Schwindenhammer¹, Sebastian Bauer¹, Florian Grabellus¹, Georg Taeger¹

¹) University Hospital Essen, Germany

Background: Isolated limb perfusion with TNF-alpha and Melphalan has proven to be a valuable tool in the treatment of locally advanced soft tissue sarcoma. Limb salvage rates for soft tissue sarcoma range above 80% in the current literature. Liposarcomas make up for almost 20% of all STS. In recent times the understanding of the different sub entities of liposarcomas has improved greatly. This retrospective study was conducted to clarify how the different sub entities of liposarcoma respond to isolated limb perfusion.

Methods: In our ILP-database we identified 125 cases of patients with soft tissue sarcoma who received subsequent resection after ILP to allow for an analysis of histopathologic regression of the tumor. We reviewed the histopathologic results from resection specimen, addressing the question of grade of regression of the tumor and resection margins.

Results: Out of the total of 125 patients 23 (18%) suffered from liposarcomas. There were two cases of high differentiated liposarcoma (9%), 5 cases of myxoid liposarcoma (22%), another 5 cases suffered from dedifferentiated liposarcoma (22%), there were 10 cases of myxoid round cell liposarcoma (43.5%) and 1 case (4.3%) of pleomorphic liposarcoma.

In the liposarcoma collective the mean regression of the tumor after ILP was 73.7% (median: 89.0%; std. deviation: 32.1). The analysis of all other sarcomas revealed a mean regression of 77% (median: 94.6%, std. deviation: 31.8). Analysis of cross tables revealed a positive response (less than 10% of vital tumor) in 52% of liposarcomas compared to 60% positive response for all other sarcomas.

Analysis of sub groups from the liposarcomas revealed that myxoid round cell liposarcoma responded best with 70% (7 responders vs. 3 non-responders), myxoid liposarcoma responded in 60% (3 responders vs. 2 non-responders). Interestingly, dedifferentiated liposarcoma responded in only 40% (2 responders vs. 3 non-responders). The two cases of high-differentiated liposarcoma did not respond to ILP (0 responders).

Conclusion:

It appears that myxoid round cell liposarcoma and myxoid liposarcoma do respond better to isolated limb perfusion than dedifferentiated liposarcoma or pleomorphic liposarcoma. Well differentiated liposarcoma is less responsive to ILP which could be explained by its low vascularity.

E-mail (main author): lars.podleska@uk-essen.de



O1:107

Local and systemic toxicity of isolated limb perfusion

Teymuraz Kharatishvili¹, Dmitry Martynkov², Boris Narkevich², Yuri Buydenok², Alexander Fedenko², Nikolai Petrochenko², Mamed Aliev²

¹) Russian Cancer Research Center RAMS ²) RCRC RAMS, Russian Federation

Background: To estimate the toxicity using isolated limb perfusion in RCRC RAMS.

Methods: Isolated regional perfusion, according to foreign research is an effective method in treatment of soft tissue sarcoma and in-transit metastases of melanoma of the limbs. There were 20 patients treated at the RCRC in 2010-2012. Women - 17 (85%), men - 3 (15%). Mean age $47 \pm 16,7$ years, range 21 to 79 years. Perfusion of the lower limb was performed in 18 patients, upper limb - in 2 patients. Melanoma - 14 cases (stage 3B, 3C, 4), soft tissue sarcoma - 6 cases. Control of leakage in overall blood circulation was performed by dynamic radiometry. Perfusion was performed at mild hyperthermia. Overall response to treatment was recorded in 17 (85%) patients, a complete response - in 5 (25%), partial response - in 12 (60%), stabilization - in 3 patients. Limb salvage in 20 patients. Leakage during perfusion did not exceed 6% (an average of 1-2%). Evaluation of local toxicity was conducted on a Wieberdink scale. At the first two levels indicated moderate hyperemia and edema. On the third level is growing lesion deep tissue structures. At the fifth level of toxicity performed amputation. Evaluation of systemic toxicity was conducted by NCI-CTC.

Results: In our study, there was no local toxicity above level 2 (moderate redness and swelling of the limbs). None of the patients had no severe systemic toxicity due to low leakage from the isolated limb into the systemic circulation.

Conclusion: There was no significant local or systemic side effects. Thus the high treatment efficiency (up to 85% of overall response) and the ability to save the limb can be achieved without complications.

E-mail (main author): generaloncology@rambler.ru



O1:108

Isolated limb perfusion for locally advanced soft tissue sarcoma

J. Mattsson¹, R. Olofsson², P. Bergh¹, Ö. Berlin¹, K. Engström¹, B. Gunterberg¹, M. Hansson¹, P. Lindnér¹

¹ Sahlgrenska University Hospital ² Department of Surgery, Sweden

BACKGROUND: Isolated limb perfusion with Tumor Necrosis Factor alpha and Melphalan (TM-ILP) has proven to be a successful option in treating advanced soft tissue sarcomas (STS), where amputation otherwise is needed to achieve safe surgical margins.

METHODS: From 2000 to 2009, 54 patients with locally advanced STS, who all were candidates for amputation, were treated with totally 57 TM-ILP procedures and then followed prospectively. The median follow-up time was 30 months. Median tumor size was 10 cm, and 94% of the patients had high-grade tumors. TNF-alpha was administered in a dose of 3 mg in upper limbs and 4 mg in lower limbs, provided limb tissue temperature had reached 38°C. After 30 min, Melphalan (13 mg/L in upper limbs, 10 mg/L in lower limbs) was administered and the temperature increased to 40°C with a perfusion time of 90 min in total.

RESULTS: The clinical overall response after TM-ILP was 71% (including 21% CR), and 60% of the patients underwent resection of the tumor remnant after a median of 2 months. The histopathologic response rate in the resected specimens was 76%. Local recurrence/progress occurred in 37% of the patients after a median of 7 months. Thirteen patients finally underwent amputation after a median of 11 months, giving a long-term limb salvage of 76%.

CONCLUSIONS: TM-ILP of advanced soft tissue sarcoma of the extremities makes limb-sparing surgery possible in a high proportion of patients.



O1:109

New innovative treatment option of aneurysmal bone cysts with Denosumab

Tobias Lange¹, Christoph Stehling², Georg Gosheger³, Birgit Fröhlich⁴, Mark Klingenhöfer⁵, Jendrik Harges³, Heribert Jürgens⁴, Tobias Ludger Schulte³

¹ University Hospital Muenster ² Radiology ³ Orthopedics and Tumor Orthopedics ⁴ Pediatric Hematology and Oncology ⁵ Neurosurgery, Germany

Aneurysmal bone cysts (ABC) are expansible destructive tumors which are positive for markers of osteoclasts resembling Giant Cell Tumors (GCT). The treatment of ABC implies surgical resection, curettage and cavity filling, embolisation, fibrosing agent injection or radiotherapy. These options can be unsatisfactory in children and adolescents with lesions in critical locations, e.g. in the spine, implying the need for innovative therapies.

Denosumab is a human monoclonal antibody that inhibits osteoclast function by blocking the cytokine receptor activator of NFκB ligand. Satisfying results of Denosumab in treatment of GCT and the immunohistochemical similarities justify the assumption of positive effects on ABCs.

This report is the first description of a therapeutic use of Denosumab in a patient with a spinal ABC. A case of an eight years old boy with a recurrent spinal ABC at C5 after surgery with intralesional tumor resection is described. The interdisciplinary tumor board discussed the remaining treatment options, implying revision surgery, embolisation, radiotherapy, fibrosing agents and an individualized treatment without as yet scientifically proven benefit using Denosumab. Due to relevant disadvantages of surgery (unlikelihood of wide resection, undesirable instrumented fusion in a growing child), radiotherapy (risk of radiation injury) and fibrosing agents (risk of emboli), embolisation was tried, but failed due to an absence of appropriate tumor vascularization. Finally, Denosumab therapy was initiated following extensive information and written consent by the family and approval of the health service.

Denosumab was given at a dose of 70 mg/m² BSA SC q 4 weeks, the dose being adapted from the approved adult dose of 120 mg q 4 weeks. Denosumab therapy was supplemented by appropriate daily oral substitution of calcium and vitamin D.

Since Denosumab therapy started, the patient recovered significantly from pain and neurologic symptoms and is in a healthy condition with no severe side effects. MRI checkup after 2 and 4 months and CT scan after 5 months showed regression of the cystic ABC and a replacement by solid bone marrow-like tissue. A longer follow-up and clinical studies will be needed to evaluate Denosumab for patients with ABC in critical locations.

E-mail (main author): tobias.lange@ukmuenster.de



O1:110

Efficacy of gemcitabine plus docetaxel in patients with refractory osteosarcomas and soft tissue sarcomas: results of Phase II trial

Shintaro Iwata¹, Tsukasa Yonemoto¹, Hiroto Kamoda¹, Takeshi Ishii¹

¹ Chiba Cancer Center, Japan

Objective: To evaluate the efficacy and safety of gemcitabine plus docetaxel in the treatment of patients with previously treated refractory bone and soft tissue sarcomas, we conducted prospective Phase II trial.

Methods: Pediatric and adult patients with measurable solid tumors that relapsed after or were refractory to standard therapy were eligible. Gemcitabine at 675 mg/m² on days 1 and 8 plus docetaxel at 75 mg/m² on day 8 were administered every 3 or 4 weeks. The primary endpoint was the 6-month progression-free survival rate (PFSR).

Results: Thirty-one patients: 14 with malignant bone tumor (11 with osteosarcomas, 1 with angiosarcoma, chondrosarcoma, and fibrosarcoma) and 16 with soft tissue sarcoma were enrolled from January 2011 to December 2012. Median patients age was 44 years (range 8-79 years). A total of 153 courses of chemotherapy were administered (1-13 courses, median: 4 courses). The 6-month PFSR was 46.7% (95% CI, 26.6-67.9%), and median PFS was 3.3 months (0.4-15.8 months). Of 27 patients evaluable for response, there were 5 PR patients (2 UPS, 1 leiomyosarcoma, 1 osteosarcoma, and 1 fibrosarcoma) and 17 SD patients; the response rate was 18.5% and the disease control rate was 81.5%. The 6-month PFSR for osteosarcoma patients was 42.9% and that for spindle cell sarcoma of soft tissue was 59.3%; although no statistical difference was observed. The major grade 3/4 hematologic adverse event was neutropenia (70.6%). As for non-hematologic adverse event, grade 2 diarrhea was observed in 4 patients and grade 2 pneumonia and allergic reaction was observed in each 2 patients, although no treatment-related death occurred.

Conclusion: Gemcitabine plus docetaxel were associated with favorable efficacy and manageable toxicity in refractory patients with not only soft tissue sarcoma but also osteosarcoma.

E-mail (main author): siwata@chiba-cc.jp



MGL1:101

30-year experience with biological reconstruction at Kanazawa University

Hiroyuki Tsuchiya¹

¹) Graduate School of Medical Science, Kanazawa University, Japan

The progress of musculoskeletal sarcoma treatment has been providing the improvement of limb-saving surgery and survival rate in patients with those tumors. Recently, limb-saving tumor surgery, which is not limited for merely saving, aims at much better functional results. The goal of limb-saving tumor surgery is normalization of the affected limbs in function and appearance.

Biological reconstruction after tumor resection is classified into two sub-types. One is reconstruction with living bone such as vascularized bone transfer and distraction osteogenesis. The other one is reconstruction with devitalized bone such as allograft, irradiated autograft, autoclaved autograft and frozen autograft treated by liquid nitrogen. Each reconstruction method has both advantages and disadvantages. Living bone can provide structure, cells, proteins and blood supply while most of devitalized bones can provide only structure and proteins. Biological healing of bone and excellent attachment between bone and soft-tissue can be specifically expected in biological reconstruction.

In this lecture, I would like to introduce reconstruction methods with distraction osteogenesis, massive frozen autograft and vascularized fibular graft, and also talk about tips how to make the best use of those methods based on our experience of 30 years.

E-mail (main author): tsuchi@med.kanazawa-u.ac.jp



O2:101

Biologic reconstruction after bone tumor resections in children and adolescents

Reynaldo Jesus-Garcia¹

¹ Universidade Federal de São Paulo, Brazil

Introduction

The bone sarcomas are very frequent in small children and adolescents. The osteosarcoma and Ewing's family tumors are the most common. In this age, we have to consider the growing of the bone, the distance from the tumor to the growth plate and the intense activity of the children. We do not have many options of reconstruction and the amputation, most of the times, are the indicated technique. The purpose of this study is to present our solutions when we decide do not indicate an amputation.

Material and Method

We will present in patients with open epiphyseal plates the biologic techniques of limb preservation. We indicated the reconstruction with non-vascularized fibulae, vascularized fibulae and bone elongation with Ilizarov. The patients, a few days after the surgeries resumed the chemotherapy protocol, without interruption. In some Ewing's family tumor patients, we indicated irradiation of the site.

Results

Most of the patients were submitted to non-vascularized and vascularized fibulae reconstruction in humerus, femur and tibia tumors. The fibula was secured in to the bone with screws, special custom-made plates or Ilizarov. The time until consolidation was long but the consolidation occurred in all patients. In most of the patients there was not necessary other surgeries to get consolidation but in some, the consolidation was obtained just after additional minor surgeries, for example, grafting techniques. In others, to get the consolidation, it was necessary to change the synthesis or to use an Ilizarov. As complications, we had some fractures of the grafts but in none of them, we had infection or local recurrence.

Conclusion

Before to indicate an amputation, we have to consider a biological limb salvage procedure.

E-mail (main author): rjgarcia.ops@terra.com.br



O2:102

Pedicled and free fibula grafts in primary reconstructions of the tibia: which and when?

Marco Manfrini¹, Marco Colangeli¹, Laura Campanacci¹, Massimiliano De Paolis¹, Massimo Ceruso²

¹ Istituto Ortopedico Rizzoli ² C.T.O. Firenze, Italy

BACKGROUND: The authors report their experience with vascularised fibula autograft (VFA), either free, or ipsilateral pedicled, in large tibia defects, analysing indications and results.

METHODS: From 1994, VFA was used for tibia defects in 50 patients (median age 14ys, range 8-38) with bone sarcomas. (44 cases with neoadjuvant chemotherapy, 3 with radiotherapy).

In two patients, VFA was implanted alone, in one autografts were added. In 47 cases, VFA was associated to MBA. All cases had synthesis with plates.

Defect ranged 9-22cm, involving the diaphysis in 27 cases. In 21 cases, the resection included a proximal intraepiphyseal osteotomy; in 2 patients involved a distal intraepiphyseal osteotomy.

In 24 cases contralateralVFA was harvested as free-flap and microanastomosis performed between fibular vessels and anterior-tibialis vessels of the recipient leg.

In 26 cases ipsilateralVFA, harvested through posterolateral approach opposite to medial approach used for resection, was transposed to fill the tibia defect, maintaining the vascularity.

Implant outcome was investigated on serial radiology in 45 cases with 12 months follow-up (f-up).

Function was evaluated according MSTs.

RESULTS: At median f-up of 83months, there are 42 disease-free survivors. Two patients died for toxicity and 6 of disease.

There were 5 local recurrence: three were amputated, one revised with megaprosthesis, one patient had local radiotherapy.

There were 2 infections (one in each group) necessitating implant removal: both were reconstructed (one megaprosthesis, one Ilizarov technique).

Mechanical complications (delayed union, fracture) occurred in 14 patients. Five healed without surgery. Nine patients were revised but only 2 (one in each group) had VFA removed and substituted with new grafts. These patients were the only ones with no changes in serial radiology.

Functional analysis showed 80% Excellent and Good results (78% in freeVFA and 82% in pedicledVFA).

DISCUSSION: Both free and pedicledVFA have 95% chance to maintain viability and mechanically adapt to tibia reconstructions. PedicledVFA should be the first choice in diaphyseal defects but it's also effective in proximal intraepiphyseal reconstructions. Previous radiotherapy, fractures or leg abnormalities may force to prefer freeVFA.

AssociationVFA/MBA: Serial radiological analysis demonstrates intense remodelling suggesting biological, efficient and durable reconstructions.

E-mail (main author): marco.manfrini@ior.it



O2:103

Biological Reconstruction in high grade sarcomas – Patients under 12 years old

Eduardo Sadao Yonamine¹, Élio Consentino¹, Pedro Péricles Ribeiro Baptista¹, José Donato Próspero¹, Maria Fernanda Carriel Amary¹, Karen Voltan¹, Felipe Birriel¹, Bruna Bruscharino¹

¹ Santa Casa Medical School of Sao Paulo, Brazil

OBJECTIVES

1. Present our long term follow up of Biological Bone Reconstructions after resections of high grade sarcomas close to the growth plate.
2. Autologous bone reconstruction and long term follow up (14 - 312 months - average 173 months)
3. Safe resections and reconstructions close to the growth plate.

METHODS

- From June 1984 to June 2010, we treated 262 patients with High Grade Sarcomas (178 osteosarcomas and 84 Ewing's Sarcoma) in Santa Casa Medical School of Sao Paulo (Brazil) and The Hospital Alemao Oswaldo Cruz of Sao Paulo (Brazil)
- We exclude all cases treated in Pelvic Girdle, Pectoral Girdle, Spine, hand, forearm, foot, cases treated exclusively by radiation therapy and cases that were reconstructed by endoprostheses or don't need reconstruction (fibular cases)
- Considering 53 cases (27 Osteosarcoma and 26 Ewing's Sarcoma) in lower and upper limb submitted to resection and exclusively treated by surgery and autologous bone reconstructions.

RESULTS

- We analyse all 53 cases with limb salvage surgery and follow up from 14 - 312 months - average 173 months).
- Epidemiology: 36 males and 17 females, age: 5 to 12 years old (average 11,2), 26 cases in Femur, 17 in tibia and 10 in humerus.
- All 53 cases were treated with diaphyseal or metaepiphyseal or transphyseal resections close to the growth plate and reconstructions with autologous bone from fibula or iliac crest . 36 Non vascularized reconstructions, 13 fibular vascularized reconstructions and 4 cases of transposition from fibula to tibia.
- Complications:
 - 16 with fractures or delay of consolidations: 9 need 1 new procedures to include more iliac crest, 5 need 2 new procedures to include more iliac crest and 2 need 3 new procedures to include more iliac cres.
 - 3 case of superficial infections: treated with antibiotic therapy.
 - 2 case recidive in diaphyseal segment and were submitted to revision with endoprostheses.
 - 1 case recidive in soft tissue mass, resected and adjuvant radiation therapy.
 - 4 cases death with pulmonary metastasis, no local recurrence.
 - 1 case had cerebral metastasis after 67 months post surgery, no local recurrence.
- All 48 remaining cases still alive and had consolidations and doesn't need any kind of support.

CONCLUSION

We considering diaphyseal or metaphyseal or transphyseal resections safe even when the lesion is close to the growth plate and bone autologous reconstructions may offer long-standing reconstructions even in High Grade Sarcomas in pediatric patients (follow up: 14 to 312 months, average 173 months).

E-mail (main author): esy.pfs@gmail.com



O2:104

A new Score for the evaluation of radiographic and functional outcomes of custom made tumoral prosthesis.

Reynaldo Jesus-Garcia¹

¹) Universidade Federal de São Paulo, Brazil

Introduction

Local control of tumors is achieved with resection followed by replacement by non-conventional endoprosthesis. The Literature has many publications on the best score to assess the long-term follow-up of conventional joint replacements. Each joint, among them the knee, hip and shoulder, has several scores attempting to analyze and evaluate the functional and radiographic outcomes. Despite the use of unconventional endoprosthesis for several years for treatment of bone tumors we did not find a specific index for its evaluation regarding clinical and surgery outcomes.

Objective

The objective of this study is to carry out a score for the evaluation of non-conventional endoprosthesis used for treatment of bone tumors around the shoulder, hip and knee, based on the questionnaires and scores used in conventional knee prostheses.

Methods

We review the English Literature related to the scores for assessing follow-up concerning function, complications of the prosthesis and clinical outcomes.

Results

We compared the most useful questionnaires for conventional joint replacement and proposed a new one to patients submitted to non-conventional endoprosthesis. We identified the parameters that are not addressed satisfactorily in the assessment of a patient treated surgically by means of non-conventional endoprosthesis. This will allow us to evaluate the results of the prosthesis.

Regarding the assessment rates of patients with bone tumors, the questionnaires TESS and MSTs were suitable for comparison of patients before and after treatment but not for the evaluation of endoprosthesis.

Conclusion

Current Literature do not use a specific "score" in order assessing the outcome of non-conventional endoprosthesis used for the treatment of patients with primary tumors.

E-mail (main author): rjgarcia.ops@terra.com.br



O2:105

Autobiologic reconstructions with vascularized fibula grafts revisited.

Functional evaluation and a long-term follow-up (>10 years)

Örjan Berlin¹, Peter Bergh¹, Björn Gunterberg¹, Jonas Lundberg², Hans Mark²

¹⁾ Sahlgren University Hospital (1) ²⁾ Sahlgren University Hospital (2), Sweden

Background

Limb-sparing surgery with preserved joint-function in children with immature skeleton can be performed using vascularized fibula grafts (VFGs).

Material

1. A nine-year-old girl with a IIA osteosarcoma of the distal femur had chemotherapy (ISG-SSG I). In 2000-09 her distal femur was resected and dual VFGs were used for reconstruction. The cruciate-ligaments were reconstructed using the LCL and BF tendon. Functional score (FS) at 3-y-postop; 20/30. Follow-up (12 years): Epiphyseodesis was performed when leg-length-discrepancy was 4.5 cm. An anterior dislocation of the VFGs led to resection of the distal femur and a Mutars prosthesis (2007-09). FS with the original reconstruction was 20/30. Leg length discrepancy has been reduced (callusdistraction). 12-y-postop the FS is 26/30.
2. A nine-year-old girl with a IIB Ewing sarcoma of the proximal femur had chemotherapy (Euro-Ewing). In 1999-07 20 cm of her proximal femur was resected and dual VFGs were used. The hip joint-capsule was sutured like a pouch around the fibula head. Restriction of motion was maintained for 18 months postoperatively with an external orthosis. FS 4-y-postop was 23/30. Follow-up (13.5 years): The fibula head has remodeled into a cœfemoral head. FS was 26/30 after leg-lengthening (callusdistraction).
3. A six-year-old girl with a IIB telangiectatic osteosarcoma of the proximal humerus had chemotherapy (ISG-SSG I). 1999-11 10 cm of her proximal humerus was resected and a VGF was used for the reconstruction. The long biceps brachi tendon was sutured to the LCL and distal end of the BF tendon. The remaining rotatorcuff was sutured like a pouch around the fibula head. She had thoracobrachial plaster for 12 weeks postoperatively. FS 2-y-postop was 26/30 and 29/30 at 5 years. 6-y-postop she presented with a soft tissue recurrence in the triceps brachi muscle. After pre-operative chemotherapy a local excision was performed (2006-05). Follow-up (13 years): there are no signs of local or distant recurrence and her FS is 26/30.

Conclusion

Autobiologic reconstructions with preserved joint function is a viable option to extendable prostheses in children with bone sarcomas of the immature skeleton. Among the large joints the functional rank order of success seem to be shoulder>hip>knee.

E-mail (main author): orjan.berlin@gmail.com



O2:106

Limb salvage surgery for malignant tumors in proximal tibia involving fibula

Xiaodong Tang¹, Wei Guo¹, Rongli Yang¹, Shun Tang¹, Sen Dong¹

¹Peking University People's Hospital, China

A retrospective study of patients with malignant tumors in the proximal tibia involving the fibula was carried out to evaluate the effect of limb salvage surgery. The oncologic results, complications, and postoperative function were summarized.

Methods

Thirty-two patients were included in the study. There were 21 males and 11 females, with a mean age of 23.4 years old. The pathological diagnosis included 23 osteosarcomas, 5 chondrosarcomas, 1 malignant giant cell tumors, and 3 soft tissue sarcomas. During the operations, all patients had ligation of anterior tibial vessels, and 6 patients had resection and reconstruction of posterior tibial artery for direct tumor invasion or injury during resection. Among them, 3 patients had vessel anastomosis and 3 patients had vascular autograft with great saphenous vein. The common peroneal nerve in 4 patients and deep peroneal nerve in 5 patients were resected, respectively. The reconstruction methods included 25 endoprosthesis replacements, 5 allograft-prosthetic composite replacements, and 3 recycled tumor bearing bones.

Results

After a mean follow-up of 39.4 months, 6 patients (18.8%) had local recurrence, and the overall 5-year survival rate was 51.2%. Sixteen patients had no evidence of disease, fourteen patients were died of disease, and two were alive with disease. Variant complications occurred in 15 patients (46.9%), which included peroneal nerve palsy, ischemia of the lower leg, wound healing problem, deep infection and paraprosthesis fracture. The functional outcomes of a mean MSTS 93 score was 21.6 points (72%).

Conclusion

The indications of limb salvage surgery for malignant tumors in proximal tibia involving fibula should be restricted. Although complications encountered frequently, most patients have acceptable postoperative function.

E-mail (main author): bonetumor@163.com



O3:101

The Role of Structural Allografts in Limb Salvage Surgery - A 22 Year Perspective

William Ward¹, Thomas Rusher¹, Fred Dorey¹

¹ Guthrie Clinic, United States

A number of studies evaluating limb salvage surgery have reported a higher complication rate with allografts compared to endoprostheses, especially as regards the rate of infections, fractures and non-unions. However unique anatomic and structural conditions continue to present themselves for which structural allografts are particularly suited. The authors therefore reviewed the senior surgeons 22+ years of personal experience in orthopedic oncologic and similar limb salvage reconstructions to compare the results of structural allografts and endoprostheses in complex reconstructions requiring structural bone restoration.

The surgical case logs of the senior surgeon over a 22+ year period was queried. There were 224 massive bone reconstructions (188 bone tumors, 36 other entities) employing massive tumor-type endoprostheses (172) or major cortical structural allografts (52). The records were reviewed to determine the ultimate outcome in these reconstructions in terms of joint preservations, reoperations, major revisions and subsequent amputations.

The reoperation rate was 50% for the allografts compared to 29% in the endoprostheses ($p=0.005$), the major revision or conversion rate was 23.1% for allografts and 7% for endoprostheses ($p=0.001$), and the amputation rate was 3.8% for massive allografts and 4.1% for massive endoprostheses. Use of allografts allowed preservation of the entire native joint in 25 (48%) the majority of the native joint (all but one condyle) in 8 joints (15%) and allowed 16 hemi joint preservations (31%) compared to 2 complete joint preservations (1%) and 99 hemi joint preservations (58%) with endoprostheses ($p=0.001$).

The revision rate for allograft reconstruction was much higher than that for endoprosthetic reconstruction: however, the allograft reconstructions in the majority of these specific cases allowed bone stock restoration and greater native joint preservation in ways that no endoprosthesis could accomplish without further bone or joint loss or compromise. The ultimate long-term limb salvage rate of 96% with either method of reconstruction confirms the applicability of allograft reconstruction in selected cases. The additional benefit of preserved growth plates was occasionally also accomplished with allograft reconstructions. Specific examples will be presented.

E-mail (main author): Ward_William@Guthrie.org



O3:102

More than thirty years follow-up of first generation proximal femur reconstruction.

Björn Gunterberg¹, Örjan Berlin¹, Peter Bergh¹

¹) Sahlgrenska University Hospital, Sweden

Background: At the first meeting of what became the ISOLS (1981) Bertil Stener presented a way to reconstruct the proximal femur after tumor resection using a long-stem Moore prosthesis surrounded by a cement spacer substituting the resected part of the bone. The method was, in the hands of others, modified and changed over the years without any solid basis for doing so. This small study was initiated by the admission of a patient who following trauma had a dislocated and bent prosthesis, implanted 36 years previously, according to the original method.

Patients and methods: Eleven consecutive patients with the original reconstruction and with a follow-up of 31-38 years were reviewed. Seven had metastatic lesions and 4 primary tumors. The average age at surgery was 48 years. Six were men, 5 women. The surviving patients were interviewed and had radiographic examinations.

Results: All patients with metastatic lesions were dead, mean survival 16 months. All 4 patients with primary tumors were alive, mean follow-up 36 years. One patient with a local recurrence had hemipelvectomy. The only revision was because of trauma 36 years postoperatively. The other two patients had SMTS scores of 63 percent and 93 percent.

Conclusion: The described method for reconstruction of the proximal femur after tumor resection can be characterized as safe, simple and swift. It is very cheap and particularly suitable for metastases but has proven successful in locally aggressive lesions and low-grade malignant tumors with more than 30 years follow-up.

E-mail (main author): bjorn.gunterberg@telia.com



O3:103

Reverse shoulder prosthesis after resection of the proximal humerus for bone tumours

Anne Kaa¹, Peter Holberg Jørgensen¹, Jens Ole Søjbjerg¹, Hans Viggo Johansen¹

¹Aarhus University Hospital, Denmark

Background:

The purpose of the present study was to investigate/evaluate the functional outcome in patients who had a reverse shoulder prosthesis implanted after removal of a proximal humeral bone tumour. All patients operated on between 1998 and 2011 at the department of orthopaedic surgery, Aarhus University Hospital, were included.

Methods:

Registrations: age, gender, type of tumour (primary or metastatic) and classification, concomitant diseases, associated fracture, amount of humeral bone resection, surgical margins, extent of additional soft tissue resection, adjuvant treatment and surgical complications.

Examinations: Range of movement, MSTS (Musculo Skeletal Tumour Society) score and TESS (Toronto Extremity Survival Score)

Results:

From 1998 to 2011 a total of 16 patients were operated. At follow-up five patients had died and one lost to follow-up, leaving 10 patients for examination. Mean age at follow-up was 42 years (19 to 79). The mean follow-up was 46 months (12 to 136 months). Eight patients had a primary and two patients a secondary bone tumour. Two patients had superficial infections. One patient had a deep infection and the prosthesis was removed. The prosthesis loosened in two patients. One prosthesis dislocated twice. All patients had some degree of atrophy or pseudoatrophy of the deltoid muscle.

The average range of movements (ROM) was: Abduction: 78° (range 30° to 150°). Flexion: 98° (range 45° to 180°). External rotation: 32° (range 10° to 60°). Internal rotation: 51° (range 10° to 80°). The mean MSTS score was 77% (range 60 to 90%) and mean TESS score was 70 % (range 30 to 91%).

Conclusion:

Use of the reverse shoulder prosthesis in tumour patients yields acceptable results in terms of shoulder function. Patients report good active range of motion and shoulder function.

E-mail (main author): kaa.anne@gmail.com



O3:104

The Outcome of Total Humeral Endoprosthetic Reconstruction for Bone Tumours

Hazem Wafa¹, Robert Grimer¹, Simon Carter¹, Roger Tillman¹, Lee Jeys¹, Adesegun Abudu¹

¹ The Royal Orthopaedic Hospital, United Kingdom

Aim of the work: To evaluate the functional and oncological outcome of total humeral endoprosthetic reconstruction after bone tumor resection.

Material and Methods: Twenty six patients (8 males and 18 females) with a mean age of 30.4 years (range, 8.9 to 86 years) were included in this study. Histological diagnosis was osteosarcoma in eleven patients, chondrosarcoma in six, Ewing's sarcoma in four, metastatic carcinoma in three, liposarcoma in one, and giant cell tumor of bone in one remaining patient. Twenty two patients had their total humeral endoprosthetic replacement for primary reconstruction while the remaining four patients received their implants for failed other reconstructive techniques.

Results: At a mean followup of 7.4 years (range, 3 months to 25.9 years), eleven patients were alive with no evidence of disease, while eleven of the remaining fifteen died with metastatic disease. Local recurrence was seen in five patients (19.2%) and all eventually died of disease progression. Two patients (7.7%) developed deep periprosthetic infection and both elected to receive prolonged antibiotic suppression with implant retention. According to the Kaplan-Meier survival analysis, the cumulative ten-year implant survival was 91.3%. The mean MSTS functional score at the time of the latest followup was 83.3% (range, 60-93.3%).

Conclusions: Total humeral endoprosthetic replacement is a reliable method of reconstruction after tumor resection with excellent long term survival, satisfactory functional outcome, and a low complication rate.

E-mail (main author): hazem.wafa@nhs.net



O3:105

Tumor endoprosthesis replacement after extraarticular knee resection in bone and soft tissue tumors

Jendrik Hardes¹, Marcel P. Henrichs², Sebastian Bockholt², Georg Gosheger³, Wiebke Guder², Markus Nottrott², Helmut Ahrens², Dimosthenis Andreou², Arne Streitbürger²

¹) University Clinic of Muenster, Germany ²) ³), Germany

Background: Most studies dealing with tumor prostheses around the knee describe their results after intraarticular tumor resection. The aim of this retrospective study was to report the results of tumor prostheses after extraarticular knee resection.

Methods: We evaluated the clinical results and complications after extraarticular resection of the distal femur and / or proximal tibia and reconstruction with a tumor endoprosthesis (Mutars®) used in 59 patients (mean age 33 years) with a malignant bone or soft tissue tumor.

Results: Limb survival was 80% after a mean follow-up of 53 months. Periprosthetic infection was the most common cause for secondary amputation (eight patients). Prosthetic failure was mainly caused by periprosthetic infection in 37%, aseptic loosening in 17% and periprosthetic fracture in 10% of patients. Wear of the bushings made a minor revision necessary in 20% of patients. The mean musculoskeletal tumor society score was 23 (range; 10 to 29). An active extension gap over 10° was obvious in ten patients.

Conclusion: Our results suggest that limb salvage with tumor prostheses after extraarticular resection can achieve good functional results in the majority of patients, but the complication rate and secondary amputation rate is higher compared to patients treated with an intraarticular resection.

E-mail (main author): hardes@uni-muenster.de



O3:106

Functional reconstruction of total femur with megaprotheses

Domenico Andrea Campanacci¹, Filippo Frenos¹, Antonio Vilardi¹, Giuseppe Caff¹, Marco Planta¹, Giovanni Beltrami¹, Guido Scoccianti¹, Rodolfo Capanna¹

¹Azienda Ospedaliera Universitaria Careggi, Italy

Background: Total femur reconstruction with megaprotheses may be performed after bone tumor resections or in extensive bone loss due to multiple revisions or posttraumatic sequelae. The major concerns are infection, hip instability, due to the loss of all muscular insertions, and long term durability of the articular hinge of the knee and tibial stem, subject to high stresses due to the long lever arm. The objective of this study was a retrospective evaluation of total femur megaprosthesis, with the aim to evaluate morbidity of the procedure, implant survival and functional results.

Methods: From 2001, 20 patients underwent total femur resection and reconstruction with MegasystemC® (Waldemar Link®, Hamburg, Germany) modular prosthesis. There were 11 males and 9 females with an average age of 51 years (11-81). The diagnosis was a bone tumor in 15 cases (primary malignant 11, metastatic 3, benign 1), while in 5 the total femur replacement was performed after prosthetic failure (tumoral prosthesis 3, conventional hip and knee prosthesis 1, septic revision 1). In 3 patients an allograft-prosthesis composite was performed (proximal femur allograft 1, autograft 1, proximal tibia allograft 1). In one case with extensor apparatus insufficiency, total femur prosthesis with knee arthrodesis was performed.

Results: The average follow up was 40 months (1-126). Two major complications occurred in the same patient: wound dehiscence with superficial infection healed after a surgical debridement and hip dislocation treated with closed reduction. In 1 case a local recurrence occurred requiring a hindquarter amputation. Implant survival with surgical revision or amputation as end point was 88.7% at 5 and 10 years. The functional result of evaluable patients, according to MSTs, showed an average score of 63% (40%-86%).

Conclusion: Total femur reconstruction with Megasystem C showed to be an effective limb salvage procedure in extensive bone loss after tumor resection or prosthetic revision. Despite the concerns about infection risk reported in literature after this procedure, in our series the infection rate was 5%. In conclusion, total femur modular prostheses are a successful solution in selected clinical situation but additional long term studies are required to better define implants' durability.

E-mail (main author): campanaccid@gmail.com



O3:107

Total femur prostheses for reconstruction after resection of sarcomas.

Pietro Ruggieri¹, Gabriele Drago¹, Elisa Pala¹, Giulia Trovarelli¹, Teresa Calabrò¹, Andrea Angelini¹, Carlo Romagnoli¹

¹) University of Bologna, Istituto Rizzoli, Italy

Background. The choices of treatment for patients with extensive tumors of the femur include total femur mega-prosthesis or large allograft-prosthetic composites. Previous reports suggest variable survival ranging from 60-70% at 1 to 2 years. However, these studies described earlier prostheses and techniques. To confirm previous reports we determined risk of local recurrence, overall survivorship and function in patients with total femur reconstructions for tumors.

Methods. We retrospectively reviewed 26 patients with total femur megaprotheses implanted between 1987 and 2010 after resection of bone tumors. Two patients lost at followup were excluded; the remaining 24 included 15 males and 9 females with a mean age of 27.2 years. The mean followup was 5.3 years (range, 5 months - 23 years). Function was assessed according to the MSTS system II.

Results. One patient developed a local recurrence during followup (4.1%). At last followup, ten patients were continuously disease free at a mean of 11.1 years, one patient had no evidence of disease after treatment of a recurrence, another patient had no evidence of disease after treatment of a pulmonary metastasis, and 12 patients died of their disease at a mean time of 1.5 years. In 21 patients evaluated with the MSTS score, the mean score was 68.41%; seven patients had over 75%, eleven from 51% to 75%, three from 26% to 50%. Four patients (16.6%) had complications requiring further surgery in absence of trauma. A fifth patient had a post-traumatic periprosthetic fracture.

Conclusions. A total femur prosthesis allows a limb-preserving procedure in tumors with extensive femoral involvement or in the presence of a skip lesion along the femur. The prognosis of these tumors requiring total femur resection is poor, but this reconstruction provides good function with a relatively low rate of major complications.

E-mail (main author): pietro.ruggieri@ior.it



O3:108

Mid-term results after MUTARS prosthesis in the distal femur and proximal tibia reconstruction: a retrospective study in 97 patients

D.T. Mensch¹, R. Mahdad¹, L. Bollen¹, M.A.J. van de Sande¹, A.H.M. Taminiau¹, P.D.S. Dijkstra¹, R.G.H.H. Nelissen¹

¹Leiden University Medical centre, Netherlands

Background

The use of the Modular Universal Tumour And Revision System (MUTARS®) is widely accepted for limb salvage and reconstruction in which Leiden University Medical Centre (LUMC) has over 15 years of experience.

Methods

A retrospective study was conducted on all cases concerning reconstruction of the distal femur and proximal tibia, focusing on failure mechanisms and contributing factors thereof in mid- to long-term follow up after primary MUTARS implantation without silver coating. A database was compiled of all 118 patients operated in the LUMC of which 97 cases more than two years after primary MUTARS implantation were included in our current study.

Results

97 cases were included, 55% male subjects with a mean age at surgery of 40 years (14-89) and median follow-up 98 months (2-204). 76 prosthesis were implanted for distal femoral defects, 21 for proximal tibial defects. Indications for implantation included primary malignancies in 72%, mainly Osteosarcoma (47%) and chondrosarcoma (9%). Other indications included failed previous oncologic reconstructions (21%), Giant Cell Tumours (5%), Metastasis (1%) and non-union after fracture treatment (1%).

68 complications in total were recorded in 62 cases leading to one or more reoperations in 52 cases. Mechanical failure was seen in 20% of all cases, 56% (9/16) of non-hydroxyapatite coated stems versus 12% (10/81) of hydroxyapatite coated stems, demonstrating a significant preventative factor in mechanical failure with p-value Infection was seen in 13% of cases, wherein a non-significant trend toward more complications was seen concerning tibial implants, p-value = 0,32 , HR 1,8 (CI 0,6-5,9). Median time to infection for both locations combined was 6,5 months (0-131).

14 reoperations were indicated for either failure of locking mechanisms or liner-wear.

Survival function analysis demonstrated a median survival of prosthesis of 70,8 months.

Conclusion.

After MUTARS endoprosthesis reconstruction of the distal femur and proximal tibia we found a mechanical complication rate of 20% and infection rate of 13%. Hydroxyapatite coating of the stem significantly prevents mechanical failure.

E-mail (main author): dtmensch@gmail.com



O4:101

Massive Pseudotumors that Occur Around Implanted Devices.

Scott Nelson¹

¹⁾ University of California, United States

Much change and progress has occurred in the design of implanted devices used for degenerative change as well as in limb salvage surgery. In addition to aseptic loosening of components, other complications including likely hypersensitivity reactions and the formation of so-called pseudotumors are known to occur, especially with metal on metal bearings. These can be quite large and destructive, often described as being “sarcoma-like”, and management can be challenging. The spectrum of changes including typical wear, hypersensitivity, and the formation of large pseudotumors is discussed.

E-mail (main author): SDNelson@mednet.ucla.edu



O4:102

A comprehensive study of 214 osteosarcomas of the jaws

Philippe Brunner¹, Daniel Baumhoer¹, Serenella Eppenberger¹, Jan Smida², Michaela Nathrath², Gernot Jundt¹

¹ University Hospital Basel, Switzerland ² Helmholtz Zentrum Muenchen, Germany

Background:

Osteosarcomas of the jaws account for approximately 5% of all osteosarcomas and seem to represent a clinically and prognostically distinct subgroup. However, due to the rarity of the disease rather small series have been described in the literature so far.

Methods:

214 gnathic osteosarcomas, registered in the Bone Tumor Reference Center in the past 40 years, were histologically re-evaluated and graded. Additionally, the corresponding clinical files were collected and analyzed for clinico-pathological characteristics.

Results:

Our series included 136 mandibular and 78 maxillary osteosarcomas with a median patient age of 39 years and an average follow-up of 59 months. The overall survival at 5-years was 66.8% and at 10-years 59.2%, respectively. The prognosis of patients differed significantly with regard to tumor grade ($p = 0.027$), metastatic ($p < 0.0001$) and recurrent ($p < 0.0001$) disease as well as with the achievement of a complete resection (R0) at any time during the course of the disease ($p < 0.0001$, 5-year survival 79.9% vs 24.3%). Tumor size and site, however, did not prove to be of statistical significance. Interestingly, (neo-)adjuvant therapy did not prolong survival.

Conclusions:

Osteosarcomas of the jaws have distinct clinico-pathological properties compared with their counterparts in the peripheral skeleton. The mainstay of therapy seems to be the complete surgical resection of the tumor resulting in an excellent prognosis of patients.

E-mail (main author): PhBrunner@uhbs.ch



O4:103

Does amputation offer survival-benefit over limb-salvage in patients with Osteosarcoma with poor chemo-necrosis and close margins?

Krishna Reddy¹, Louie Gaston¹, Rajpal Nandra¹, Robert Grimer¹

¹Royal Orthopaedic Hospital, United Kingdom

Introduction:

Despite advances in neo-adjuvant treatment for osteosarcoma, some patients have a poor response to chemotherapy. The prognosis in this group is considerably worse than those with a good response. Poor responders will generally have larger tumours. The dilemma that often arises is whether to do limb salvage with a narrow margin of excision or an outright amputation. If limb salvage is carried out with a close margin, does post-operative radiotherapy make any difference? This study aims to address these questions.

Material and methods:

All patients with limb osteosarcoma, poor response to chemotherapy ($\leq 90\%$ necrosis), and either inadequate margins on limb salvage (marginal or intra-lesional) or primary amputation were identified from a prospective database. This group was investigated in terms of overall survival and local control.

Results:

386 patients were included in the study (139 amputation, 206 limb salvage with marginal margins, 41 limb salvage with intralesional margins). Local recurrence (LR) developed in 16 (29%) with an intralesional margin, 42 (20%) of those with a marginal margin, and 10 (7%) with an amputation. Post-operative radiotherapy was used in 42 patients. The risk of LR in this group was 28% compared to 23% for those who did not have radiotherapy. The overall survival for the whole group was 40% at 5 years. The 5-year survival was 46% in those with marginal margins, 28% in those with an amputation, and 27% for those with an intralesional margin. In 21 patients who developed LR and synchronous metastases, none survived beyond 5 years. Patients who had limb salvage and then developed LR without metastases, had identical survival as patients who had primary amputation without subsequent LR.

Conclusion:

A marginal resection of osteosarcoma with a poor response to chemotherapy carries a poor overall prognosis. However, carrying out an amputation to avoid the risk of local recurrence offers no obvious survival benefit. The role of post-operative radiotherapy in these patients remains unclear.

E-mail (main author): k.reddy@nhs.net



O4:104

Local recurrence in Ewing's sarcoma after good response to chemotherapy: disease or treatment?

Anna Price¹, Jakub Kozdryk¹, Robert Grimer¹, Lee Jeys¹

¹Royal Orthopaedic Hospital, United Kingdom

Introduction

Whilst Ewing's sarcoma is a rare malignancy it has attracted significant scientific attention due to its tumour specific translocations. Despite this flurry of research, survival curves for patients have plateaued over the last 10 years. In some cases, in spite of successful chemotherapy responses and aggressive surgical resection there are still local recurrences (LR). Local recurrence has a poor prognostic indication often leading to subsequent surgery and in many cases death from metastases. Recent data has highlighted a surprising high rate of LR even in good responding tumours.

Methods

We conducted a retrospective review of patients seen in our tertiary referral centre since 1971. 770 patients were identified with Ewing's sarcoma. 213 patients had necrosis greater than 90% who underwent surgery. 73 patients (9.4%) were identified with local recurrence of Ewing's sarcoma. In this sub-group 13 patients (17%) had isolated locally recurrent disease and at a mean of 34.2 months from diagnosis.

Results

There were 11 males and 2 females. The site of Ewing's sarcoma varied greatly but most were limb, (n=11) the most common site being the femur (n=3) followed by the fibula (n=2). All patients had neo-adjuvant chemotherapy and achieved greater than >90% necrosis. 9 achieved a 100% response. Only one patient diagnosed in 1986 received pre-operative radiotherapy (pelvis) and none underwent post-operative radiotherapy. Two patients had intralesional margins (one patient with Ewing's sarcoma of the pelvis and pre-op radiotherapy, one patient with an endoprosthetic replacement but >95% necrosis). Mean time to local recurrence was 34.2 months (11-150, n=13). One patient developed local recurrence after 12yrs. 6 patients subsequently developed metastases. 7 patients died, 5 with metastases, 1 of septicaemia and 1 cause of death was unknown. The mean radiographic volume at diagnosis was 240.92mls (range= 44.93-609.76) compared to a mean resection volume of 87.04ml (range=14.7-286.03).

Conclusion

Despite a good chemotherapy response, local recurrence is still occurring. We believe that residual microscopic disease is being left behind following conservative surgery and there is a role for either radical excision of pre-chemotherapy volume or adjuvant radiotherapy despite good surgical margins and 100% necrosis.

E-mail (main author): anna.price2@nhs.net



O4:105

Risk Stratification and Pattern of Cardiotoxicity in Pediatric Ewing's sarcoma

Emad Moussa¹, Manal Zamzam², Zeinab Salah², Ranin Soliman², Lina Gaber², Sameera Ezzat², Iman Attia²

¹ The Children's Cancer Hospital-Egypt ² CCHE, Egypt

Background: Improved therapies for childhood cancers have increased the number of survivors; however, they are prone to adverse effects. One of the common effects of treatment is cardiac dysfunction resulting mainly from therapy with anthracyclines.

Patients & Methods: Ewing's Sarcoma patients at Children's Cancer Hospital Egypt (CCHE) from July 2007 till December 2011, were retrospectively evaluated for the incidence, pattern, and severity of cardiotoxicity. Echocardiographic findings at baseline, throughout treatment, and latest follow-up in December 2012. Severity of cardiac disorders were based on Common Toxicity Criteria, 2010. Onset was classified into, acute (developed during protocol treatment), early (within one year from end of treatment), or late (after one year from end of treatment). **Results:** One hundred and forty nine patients, were treated according to Ewing's sarcoma protocol with alternating courses of vincristine, doxorubicin, cyclophosphamide and Ifosphamide , etoposide with mean age at presentation of 10 years (2-18), 88 males (59%) and 61 were females (41%). 39 patients (26%) developed cardiotoxicity as evaluated by echocardiography based on reduced left ventricular (LV) systolic performance evidenced by reduced ejection fraction (EF%) and fraction shortening (FS%). A statistical significance between the mean EF at initial presentation (mean = 66.6%) and the mean of the lowest EF (mean = 43.6%), was found (p-value < 0.001), with a mean time to develop cardiotoxicity at 17 months (5 - 49 months). The onset of cardiotoxicity was acute in 17 patients (11.4%), early in 14 patients (9.4%), and late in 8 patients (5.4%).

According to the percentage of decline in EF based on CTC criteria, it was found that 13 patients (33%) were classified as grade I (EF drop <10% from baseline), 16 patients (41%) were grade II (EF Drop 10-19%), 9 patients (23%) were grade III (EF Drop 20-29%), and 1 patient (3%) was grade IV (EF drop >29%).

No correlation was found between the incidence of cardiotoxicity and age, gender, onset, cumulative doxorubicin dose, and follow-up duration. However, the onset of cardiotoxicity was significantly correlated with the cumulative doxorubicin dose (p-value= 0.012). Only 4 patients received mediastinal irradiation, 2 of them developed acute cardiotoxicity post-radiotherapy.

Out of 39 patients, seventeen recieved antifailure measures, eighteen presented with clinical manifestations, while only eleven patients (28%) showed improved LV systolic performance, while 6 patients died from cardiotoxicity. The rest remained with impaired systolic function until the latest follow-up.

Conclusion: All patients were affected by dropping their EF, but not all of them (only 26%) had cardiac toxicity, the onset of cardiac toxicity was significantly correlated with cumulative doxorubicin dose. The incidence of cardiac toxicity was not correlated to presumed risk factors. About one third of patients having cardiac toxicity can be salvaged by therapy.

E-mail (main author): moussaemad1960@yahoo.co.uk



O4:106

Creating a risk based protocol for local recurrence in soft tissue sarcomas

Robert Grimer¹, Mousumi Biswas², Lucinda Billingham², Lee Jeys¹

¹) Royal Orthopaedic Hospital ²) University of Birmingham, United Kingdom

Aim: as part of the Sarcoma Optimum Follow-up Investigation (SOFI) we have been investigating risk factors for local recurrence in patients with STS.

Method: All patients treated with curative intent for a STS were identified from a prospective database. Patients with inadequate information about the primary tumour, the treatment or follow up were excluded as were patients with metastases at diagnosis or recurrent disease at presentation.

Results: Local recurrence (LR) arose in 253 of the 1457 patients (17%) in this series. The median time to LR was 20 months for low grade tumours and 12 months for high grade tumours. Risk factors for local recurrence were found to be: high grade (HR 1.78); intralesional margin (HR 3.0); age >58 (HR 1.6) and Size >10cm (HR1.8). Diagnosis and radiotherapy could not be shown to affect LR rates. Combining the four risk factors above produced an algorithm that predicted an incremental risk of LR from 8% (low risk) to 36% (high risk).

Of the 253 patients with LR, 173 developed it as the first event, but 80 had either pre-existing or synchronous metastatic disease. The overall 5 year survival was 14% for patients who had metastatic disease at or before LR, 51% for those with LR as first event and 60% for those who did not develop LR. When local recurrence was included in the model for overall survival, it remained a poor prognostic factor.

Conclusion: This model has helped establish risk factors for local recurrence and also suggests, like other recent analyses, that LR has a small but significant adverse outcome on survival. Data from this model will now be used to populate a cost/benefit analysis for the SOFI model.

E-mail (main author): rob.grimer@btopenworld.com



O4:107

What is the significance of necrosis following neoadjuvant chemotherapy in osteosarcoma?

Robert Grimer¹, David Peake¹, David Spooner¹, Lee Jeys¹, Simon Carter¹, Seggy Abudu¹, Sumathi Vaiyapuri²

¹, United Kingdom ² Royal Orthopaedic Hospital, Uruguay

It is generally accepted that the percentage necrosis following neoadjuvant chemotherapy in osteosarcoma is one of the most important prognostic factors for survival. A level of 90% is generally accepted as the cut off between 'good' and 'bad' response, but there is some lack of clarity as to whether this can be further refined by more accurate assessment of necrosis. The aim of this study was to investigate whether or not more accurate assessment of necrosis offered additional prognostic information.

Method: For many years our unit has recorded the actual % necrosis in patients who underwent surgical resection of osteosarcoma following neoadjuvant chemotherapy. All patients with non-metastatic limb osteosarcoma who underwent neoadjuvant chemotherapy and had >2years follow up were included in the analysis. Initially the % necrosis was scored as follows (100%, 99%, 95-98%, 91-95%; 90%, 80-89%, 50-79%, <50%). Gradually groups were merged until statistical significance was identified. 498 patients were included in the final analysis.

Results: On initial analysis it was apparent that there was a clear cut off below 90% with all patients doing worse. Patients with 90% necrosis had slightly better survival than those with 91-95% which was virtually the same as 95-98%, so these three groups were lumped together (90-98%). Patients with 99% necrosis had slightly better survival than those with 100% but these two groups were lumped together. The best classification was thus as follows - <89%, 90-98%, 99-100%. Using this criteria in a Cox model showed that the chances of survival were:

99-100% = 84% survival at 5 years (HR 0.26, CI 0.13-0.51)

90-98% = 68% survival at 5yrs (HR 0.45, CI 0.29 – 0.68)

<89% = 46% survival at 5 years (HR 1)

Conclusion: The actual % necrosis gives a useful idea of prognosis in patients with osteosarcoma.

Importantly, this study confirms the poor outcome for all patients with <90% necrosis but in this series 90% necrosis was equivalent to necrosis up to 98%. The best response was in those with 99 or 100% necrosis and these patients had nearly a four times better chance of cure than those patients with <90% necrosis.

E-mail (main author): rob.grimer@btpopenworld.com



O5:101

A new implant technology: iodine-coating for infection control

Hiroyuki Tsuchiya¹, Toshiharu Shirai¹, Hideji Nishida¹

¹ Graduate School of Medical Science, Kanazawa University, Japan

Background

Post-operative infection associated with implants remains a serious complication in orthopedic surgery. For example, infection rates between 5% and 35% have been described for endoprosthetic replacement of large bone defects after tumor resection despite strict antiseptic operative procedures, including systemic prophylaxis. Several biomaterial surface treatments have been proposed for reducing the incidence of implant-associated infections. We have done a basic experiment for the iodine-supported titanium. The results indicate that iodine-supported titanium has favorable antibacterial activity, biocompatibility, and no cytotoxicity. In this study, a clinical trial was performed using iodine-supported titanium implants in orthopaedic surgery.

Patients and Methods

A total of 344 patients with post-operative infection or compromised status were treated using iodine-supported titanium implants. The mean age of the patients was 49.3 years (range, 5-86 years). The mean follow-up period was 26 months (range, 3-44 months). One hundred ninety-two patients were male and 152 were female. The diagnoses included 157 cases of tumor, 56 of degenerative disease, 35 of limb deformity, 30 of infected pseudoarthrosis, 24 of fracture, 6 of osteonecrosis, 5 of rheumatoid arthritis and one of scoliosis. Iodine-supported implants were used to prevent infection in 257 patients with compromised status (diabetes, cancer, steroid treatment, open fracture etc.), and to treat active infection for 87 patients. White blood cells (WBCs) and C-reactive protein (CRP) were measured pre- and post-operatively in all patients. To confirm whether iodine from the implant affected physiological functions, plasma thyroid hormone levels were examined. Both examinations were conducted sequentially for a year. Radiological evaluations were performed regularly after the operation. The chronological changes of the iodine amount were evaluated using half pins and screws removed after completion of treatment.

Results

The following types of implants were used: 129 spinal instrumentations, 79 plates for osteosynthesis, 71 prostheses, 56 external fixation (pins and wires), seven nails and two cannulated screws. Acute infection developed in three tumor cases and one in diabetic foot among the 257 patients on preventive therapy. In one patient, infection was cured by debridement and removing only the Marlex mesh used to reconstruct chest wall while leaving the iodine-coated implants in place. Other three infected cases were also cured by intravenous administration of antibiotics only, without removal of the implants. The 87 treatment cases that underwent one-stage or two-stage revision surgery recovered without additional surgery. Median WBC levels were in the normal range and median CRP levels returned to < 0.5 within 4 weeks after surgery. Abnormalities of thyroid gland function were not detected. None of the patients experienced loosening of the implants. There were two patients with mechanical implant failure, which was treated by re-implantation. Excellent bone ingrowth and ongrowth were found around all hip and tumor prostheses. One year later, the amount of iodine on external fixation pins remained about 30%.

Conclusions

Iodine-supported titanium implants can be very effective for preventing and treating infections after orthopaedic surgery. Cytotoxicity and adverse effects were not detected.



O5:102

Total Femur Replacement - significant differences in varying indications?

Andreas Toepfer¹, Isabel Petzschner¹, Rüdiger von Eisenhart-Rothe¹

¹) Klinikum rechts der Isar der TUM, Germany

Background: Extensive bone loss of the femur is most commonly encountered after resection of malignant bone tumors or revision arthroplasty of the hip and knee.

Total femur replacement (TFR) is a possible method of treatment and allows to restore reasonable function, albeit associated with a high risk of significant complications.

The purpose of this study was to assess the functional outcomes and the complications associated with total femur replacement used in patients for both tumor-and revision arthroplasty.

Methods: We retrospectively reviewed 36 consecutive patients with total femur megaprotheses implanted in our clinic between 1995 and 2010. 14 patients were lost for follow-up, the remaining 22 included nine TFR for malignant bone tumors (6 osteosarcomas, 2 chondrosarcomas, 1 metastasis) and 13 TFR after failure of THA or TKA. Before TFR, all patients had previously undergone surgery on the affected limb (range, 1-8).

The mean follow-up was 53m. Scores to assess function and general medical well-being included MSTS- and SF-12 score. Complications were evaluated using Henderson's failure mode classification for tumor endoprotheses.

Results: There was a significant difference in all collected parameters between tumor patients and endoprosthetic patients. The MSTS score for all 22 Patients was $\bar{0}43,5\%$ (13/30), the MSTS score for the sub-group of nine tumor patients was $\bar{0}63,7\%$ (19/30), whereas endoprosthetic patients reached $\bar{0}29,5\%$ (9/30). Evaluation of the SF-12 showed a physical sum score for all 22 Patients of $\bar{0}32,3$ points. Tumor patients reached $\bar{0}38,3$ in this category and endoprosthetic patients $\bar{0}28,1$ points.

Four cases of hip dis-articulations, caused by periprosthetic infection, were not selected for a retrospective analysis and classified as failure. We recorded 20 major complications associated with modular megaprotheses (13 Type I/soft-tissue complications, 2 Type III/mechanical failures and 5 Type IV/infections) which resulted in 37 revision surgeries in 10 patients (3 tumor- and 7 endoprosthetic-patients).

Conclusions: Younger patients have better functional results and fewer severe complications.

Although total femur replacement allows a limb-sparing procedure in patients with extensive bone loss of the femur, this treatment remains a reserve procedure and should only be considered when the alternative is hip disarticulation.

E-mail (main author): toepfer@tum.de



O5:103

Retrospective Evaluation of the Incidence of Early Periprosthetic Infection with Silver-Treated Custom Megaprotheses in High Risk Patients: Case Control Study

Hazem Wafa¹, Robert Grimer¹, Simon Carter¹, Roger Tillman¹, Adesegun Abudu¹, Lee Jeys¹

¹ The Royal Orthopaedic Hospital, United Kingdom

Objective: To compare the incidence of early periprosthetic infection in high risk patients who have undergone endoprosthetic reconstruction using the Agluna silver-treated Stanmore custom megaprotheses with a control group who received a non Agluna-treated Stanmore implants.

Methods: We conducted a case control study recruiting 85 patients with Agluna-treated implants and 85 controls. There were 106 males and 64 females with a mean age of 42.2 years (range, 18.4 to 90.4 years) at the time of implant insertion. Fifty patients (29.4%) received their implants for primary reconstruction, seventy nine (46.5%) for one-stage revision, while the remaining forty one patients (24.1%) had a two-stage revision surgery for periprosthetic infection. Endoprosthetic replacements were of the distal femur (n=63), proximal tibia (n=36), proximal femur (n=19), hemipelvis (n=16), total femur (n=6), proximal humerus (n=6), distal humerus (n=2), distal radius (n=2), intercalary (n=12), while eight patients had combined femoral and tibial implants.

Results: All patients were followed up for a minimum of 6 months. Data collected during the postoperative period, and at 3, 6, 9, and 12 month post-operative visits was analyzed. The overall postoperative infection rates of the silver and control groups were 12.9% and 23.5% respectively ($p < 0.01$). Eight of the eleven infected prostheses (72.7%) in the silver group were successfully treated with debridement, antibiotics, and implant retention (DAIR) as compared to only five of the twenty infected implants (25%) in the control group ($p < 0.01$). Three patients with silver-treated implants (3.5%) and fifteen of the control group (17.6%) had chronic periprosthetic infection necessitating device removal, amputation or chronic antibiotic suppression ($p < 0.01$).

Eight of the fifteen patients (53.3%) with positive intraoperative cultures in the control group had postoperative infection versus only two of the fifteen patients (13.3%) in the silver group ($p < 0.01$). None of those eight patients in the control group had their infection resolved with DAIR procedure. The overall success rates in controlling infection with two-stage revisions in the silver and control groups were 80% and 52.4% respectively ($p < 0.01$).

Conclusions: The Agluna-treated megaprotheses are associated with lower rates of early periprosthetic infection. These silver-treated implants are particularly useful in two-stage revisions for periprosthetic infection and in those patients with incidental positive cultures at the time of implant insertion. The DAIR procedure appears to be more successful with this type of implants.

E-mail (main author): hazem.wafa@nhs.net



O5:104

Second cancers after endoprosthetic replacement: is metal bad for you?

Robert Grimer¹, Matthew Francis², Nicola Dennis², Gill Lawrence²

¹Royal Orthopaedic NHS Foundation Trust ²West Midlands Cancer Intelligence Unit, United Kingdom

Background: Patients who have endoprosthetic replacements have a large amount of metal placed in their bodies. With the passage of time metal ions may be leaked into the body. Concern over the association of metal ions and cancer has increased following recent reports in relation to metal on metal joint replacements. This study has therefore looked at the incidence of second cancers in patients who had an endoprosthetic replacement (for cancer) in the past.

Methods: All patients who had an endoprosthetic replacement at our centre have been followed up indefinitely. We identified all patients who had a second cancer, unrelated to the primary which they had the initial endoprosthesis for. The incidence of second cancer was confirmed by cross referencing these patients to the Central Cancer Registry which documents the incidence of all cancers arising in England.

Results: Between 1998 and 2004, 529 extremity bone sarcoma patients have had an endoprosthetic replacement. Patients were censored at the time of follow up or the time of death either due to the original cancer or natural causes. The follow up included 3000 patient prosthesis years. The mean age at insertion of the original prosthesis had been 30 (range 3 to 85). Of the 529 patients, 254 have died at a mean of 35 years of age and 275 are alive. There were 11 patients with a second cancer. The incidence was 1.5% at 5 years and 1.9% at 10 years after insertion of the endoprosthesis. The most common second cancer was breast cancer.

Conclusion: The incidence of a second cancer in patients who have had an endoprosthesis is 1.9% at 10 years. There is no evidence of an increased risk of second cancer in patients with an endoprosthetic replacement.

E-mail (main author): nicola.dennis@wmciu.nhs.uk



O5:105

Implantable venous port systems - prevention of infectious complications in children with bone tumors after the arthroplasty.

Maxim Rykov¹, Aslan Dzampaev¹

¹) Institute of Pediatric Oncology, Russian Federation

Background: The treatment of bone tumors in children requires numerous courses of chemotherapy. An initial problem to be solved is providing venous access: comfortable for the patient and entailing minimal risk of infections. This is particularly important to prevent infection of bone implants in the joints. The best option is fully implantable venous port systems.

Materials and Methods: From 2008 to 2012 we observed 175 children with bone tumors of extremities (aged 3 years to 17 years). Limb arthroplasty was performed in 167 patients (95.4%): in 2008 - 24 patients, 2009 - 34, 2010 - 28, 2011 - 44, 2012 - 37. The lowest age of the patient, who underwent surgery for knee replacement - 3.5 years, the shoulder joint - 4 years. We have used venous ports since 2010 and implanted them in 80 (45.2%) patients with limb bone sarcomas: in 2010 - 5 (17.8%) patients, 2011 - 39 (88.6%), 2012 - 36 (97.2%). Subclavian catheters were implanted in 96 (54.8%) patients.

Results: Infectious complications developed in 18 patients with limb endoprosthesis (10.8%). There were 3 infected implants (12.5%) in 2008, 5 (14.7%) - in 2009, 3 (10.7%) - in 2010, 4 (9.0%) - in 2011, 3 (8.1%) - in 2012. Two-step re-arthroplasty was performed in 11 (61.1%) patients, conservative treatment (antibiotic therapy with Maxipime, Amikacin, Zyvox or Cubicin) helped to keep the implants in 7 patients (38.8%). In this early - developed within 3 months after the operation - infectious complications occurred in 64.3% of patients, delayed - from 3 months up to 2 years - 24.1%, and late - over two years - in 11.6%. Catheter-related bloodstream infection developed in 28 (29.1%) patients with subclavian catheters, while in patients with implantable venous ports such infections were not noted. The most common cause of catheter-related infections - *S. epidermidis* (71,8%) and *S. aureus* (18,2%), also inoculated when infected implants.

Conclusion: The introduction of implantable venous port-systems for the treatment of child patients with bone tumors has significantly reduced the number of infectious complications and infections of limb prostheses (1.8 times).

E-mail (main author): wordex2006@rambler.ru



O5:106

Preliminary results of reverse total shoulder arthroplasty for tumors of proximal humerus

Pietro Ruggieri¹, Teresa Calabrò¹, Xin Sun¹, Caterina Novella Abati¹, Fernando Jorge¹, Matteo Romantini¹, Andrea Angelini¹

¹ University of Bologna, Istituto Rizzoli, Italy

Background: Proximal humerus is the third most common site for bone tumors. The rotator cuff needs often to be sacrificed, so it is a challenge to restore good shoulder function. The reverse total shoulder arthroplasty improved active shoulder range of motion after resection of rotator cuff.

Methods: We retrospectively reviewed 11 patients who had reverse shoulder arthroplasty (RSA) for proximal humerus tumors between 2005 and 2012: 7 females and 4 males with mean age 49.6 years (32 to 69 ys). Four patients had GCT, 5 chondrosarcoma, 2 metastases. Six patients received primary RSA while the others underwent revisions after failed primary reconstruction (allograft or prosthesis).

Results: All patients were alive and disease free at mean follow up of 31.7 months. One patient developed soft tissue recurrence at five years and was treated with electrochemotherapy. Nobody developed distant metastases. The mean functional MSTS score was 23.9. The mean active abduction was 60° (ranging 20° to 100°). Two patients had major complications requiring revision: 1 prosthetic dislocation and 1 plastic wear.

Conclusion: In our experience the use of reverse total shoulder arthroplasty for tumors of the proximal humerus is a reasonable reconstructive option at short-term follow-up. Our indication to inverse prosthesis is for resections including the rotator cuff but sparing deltoid muscle axillary nerve. If bone resection is proximal to the deltoid insertion, we use a modular inverse prosthesis; if the resection level is distal, we use a composite allograft with inverse prosthesis.

E-mail (main author): pietro.ruggieri@ior.it



O5:107

Proximal humerus reconstruction with MRS® Bioimpianti prostheses after resection of bone tumors: an analysis of 255 cases

Pietro Ruggieri¹, Teresa Calabrò¹, Andrea Angelini¹, Caterina Novella Abati¹, Elisa Pala¹, Mohammad Hassani¹, Marco Maraldi¹, Ilaria Piraino¹

¹ University of Bologna, Istituto Rizzoli, Italy

Background. Limb salvage using endoprosthesis is considered as a treatment of choice for bone sarcoma involving the extremities with relatively low incidence of major complications. Modular prosthetic reconstructions is the most frequently used type of reconstruction after resection of the humerus. Aim of this study was to review the experience of the Rizzoli with prosthetic reconstruction after resection of bone tumor in the humerus.

Methods. Between 1975 and 2010, 255 modular prostheses (alone or in association with allografts) type MRS® of the proximal humerus were implanted. Population included 154 males and 101 females with mean age 40 yrs (range 5 to 81). In two patients tumor involves humeral diaphysis, in all others the proximal part. Histology showed 91 osteosarcomas, 52 chondrosarcomas, 61 metastatic carcinomas, 10 GCT, 10 MFH, 9 Ewing's sarcoma, 22 other diagnoses.

Results. Major complications causing implant failure were infections (19 cases – 7.4%), aseptic loosening (4 cases – 1.5%) and breakages (3 cases – 1.2%). Local recurrence occurred in 8 patients (3%). Survival in patients with primary tumors was 35% at 10 and survival in patients with metastasis was 3% at 10 years. Implant survival to all major complications was more than 80% at 10 years and 20 years.

Conclusions. This prosthesis is actually a simple spacer, therefore it is indicated for resections of tumors where it is not possible to spare the abductor apparatus (deltoid, axillary nerve, rotator cuff). Otherwise we prefer different reconstructions. This simple modular prosthesis provides satisfactory results, but not abduction.

E-mail (main author): pietro.ruggieri@ior.it



O5:108

Survival of Modern Tumor Endoprostheses: complications, functional results, and a comparative statistical analysis

Pietro Ruggieri¹, Elisa Pala¹, Eric Henderson², Giulia Trovarelli¹, Andrea Angelini¹, Matteo Romantini¹, Teresa Calabrò¹

¹ University of Bologna, Istituto Rizzoli, Italy ² Moffitt Cancer Center, United States

Background: Lower limb is a frequent site for bone tumors. Due to their availability, modularity, uncomplicated usage, immediate fixation, and relatively low complication rates compared to alternatives, metallic endoprostheses have become the reconstruction option used most commonly. Complications and failures of these devices remain high compared to other arthroplasty procedures.

Objective of this study was to retrospectively analyze results of a modular reconstructive tumor prosthesis for the lower limb (GMRS-Stryker) in primary and secondary implants.

Materials and Methods: Twohundred-nintyfive GMRS prostheses were implanted: 197 primary implants, 98 revisions in 84 failed primary reconstructions after tumor resection and 14 failed implants for non oncologic reasons. Sites of reconstruction included: 199 distal femur, 60 proximal tibia, 32 proximal femur, 4 total femur. Histologic diagnoses: 166 osteosarcomas, 22 Ewing sarcomas, 22 chondrosarcomas, 18 spindle cell sarcoma, 12 other sarcomas, 6 metastases, 35 giant cell tumors. Causes of endoprosthesis failure were classified as: soft tissues failures about the implant (Type 1), aseptic loosening of the implant (Type 2), structural fracture (Type 3), infection (Type 4), and tumor recurrence (Type 5). Functional results (MSTS system) were analyzed and Kaplan-Meier curves of implant survival defined comparing primaries and revisions.

Results: At a mean oncologic follow up of 4.2 years (range, 2 to 8 years), 195 patients are continuously NED, 43 NED after treatment of relapse, 10 AWD, 33 DWD. The overall failure rate in our series was 28.8% and failure occurred at a median of 1.7 years (range, 1 month to 7 years). There was a significant difference in implant survival of all modes of failure between primary and revision implants ($p = 0.0313$). There was also significant difference in implant survival of failure of primary and revision proximal tibial implants ($p = 0.0410$). Breakage of prosthetic components did never occur. Functional scores were obtained in 229 of 295 patients. The average overall score was 81.6% (24.5 range, 5-30).

Conclusion: Middle term results with GMRS are promising, with excellent functional results and low incidence of complications. A significant difference in implant survival was found in this series between primary and revision implants. Functional results are satisfactory.

E-mail (main author): pietro.ruggieri@ior.it



O5:109

Modular prosthesis with a silver porous surface modification for periarticular reconstruction of the lower limb

Domenico Andrea Campanacci¹, Nicola Mondanelli¹, Filippo Frenos¹, Antonio Vilardi¹, Serena Puccini¹, Giovanni Beltrami¹, Guido Scoccianti¹, Rodolfo Capanna¹

¹Azienda Ospedaliera Universitaria Careggi, Italy

Background:

Infection in orthopedic surgery is a dreadful complication. Patients are often subjected to several surgeries with prolonged antibiotic treatment, and the risk of persistent infection and poor functional outcome is high. In most of cases, a residual massive bone defect is present, due to extensive debridement to remove necrotic or infected bone. The antimicrobial activity of silver ions has been known since ancient times (silver cups and cisterns for drinking water) and in recent years has been applied in everyday life (toothbrushes, underwear) as well as in medicine (wound dressings).

Methods:

Recently, an evolution of modular prosthesis MegasystemC® (Waldemar Link®, Hamburg, Germany) with a silver porous surface modification (PorAg) was developed. At our Institution, from 2010, 16 prostheses were implanted in 15 patients with a history of septic arthroplasty (7 cases, 3 hip and 4 knees) or septic meta-epiphyseal post-traumatic deformity or nonunion (6 cases, 2 proximal and 4 distal femur), and as primary reconstruction in 3 oncologic patients. There were 9 males and 6 females with a mean age of 54 years (30-75). One patient underwent only 1 surgery before resection and modular silver-coating prosthesis, while in all other revision cases the number of previous surgeries ranged from 3 to 8. In 12 cases the reconstruction was performed with a mobile joint prosthesis (6 proximal femur and 4 distal femur) and in 4 cases with a knee arthrodesis prosthesis.

Results:

Monitoring of inflammatory markers (ESR, C-reactive protein, fibrinogen) showed resolution of the infection in all previously infected cases. At a mean follow up of 13 months (1-27), 2 dislocations of proximal femur prosthesis occurred, treated with closed reduction in 1 case and open revision and new silver coated implant in 1 case. Functional results following MSTS evaluation system showed an average score of 60% (43%-90%).

Conclusion:

In conclusion, the preliminary results of MegasystemC PorAg are encouraging, although a larger series of patients with longer follow up is needed. Our experience suggests that modular prostheses with silver porous surface modification may be indicated in periarticular bone loss in septic failures and as primary oncologic reconstruction in selected patients.

E-mail (main author): campanaccid@gmail.com



O6:101

Chondrosarcoma of the hands and feet: When to worry?

Anna Price¹, Jakub Kozdryk², Robert Grimer², Lee Jeys²

¹ Royal Orthopaedic Hospital ² Royal Orthopaedic Hospital, Birmingham, United Kingdom

Background

Chondrosarcoma of the small bones in the hands and feet are extremely rare. In contrast, enchondromas are common benign lesions. Differentiating between the two can be extremely challenging. Enchondromas of the hands or feet are often not treated in specialist centres, therefore the question is, when should the surgeon worry about malignant conversion? Although metastases are relatively rare in chondrosarcomas of the hands and feet, local recurrence is common. Local recurrence can be aggressive, often ungrading from the previous tumour grade.

Methods

Our database contains information on 3657 primary bone tumours treated since 1971, of these, 804 had primary chondrosarcomas. A retrospective review was taken of the 69 patients identified with chondrosarcoma of the small bones of the hands or feet (9%). During the same period 101 patients were identified with benign enchondroma of the hands or feet. A prospectively updated database, patient notes and radiology reports were reviewed for demographic details, surgery, complications, local recurrence and survival.

Results

Of the 69 patients, 23 (33%) chondrosarcomas were in the feet, with 46 (66%) being in the hands. 8 patients had known multiple enchondromas (4 patients with Olliers, 4 patients with Maffucci syndrome).

At presentation, 31 (46%) patients had grade 1 chondrosarcoma, 32 (48%) grade 2, 2 (3%) with grade 3 and one dedifferentiated chondrosarcoma. 8 patients developed a local recurrence at a mean of 32 months (range 2-110 months), with the initial grade being grade 2 in the majority (n=8/9, one patient grade 1). 4 patients developed metastases at a mean of 78 months (range 2-250) all occurring in higher grade tumours.

There was evidence of a previous enchondroma in 52% of patients prior to presentation, suggesting malignant conversion. Most patients had radiology suggesting an aggressive process with features of cortical breach, soft tissue mass or endosteal scalloping.

Conclusion

Chondrosarcoma of the hand and feet remain rare. Patients often had previous treatment for enchondromas and aggressive radiological features. Surgeons should be wary of these features and refer to a tertiary referral bone unit for biopsy if they are present.

E-mail (main author): anna.price2@nhs.net



O6:102

Metastatic potential of low-grade chondrosarcoma of bone - results of a multi-institutional study

Dimosthenis Andreou¹, Magdalena Gilg², Mathias Werner³, Jendrik Harges¹, Daniel Pink⁴, Georg Gosheger¹, Andreas Leithner⁵, Per-Ulf Tunn⁶, Arne Streitbueger¹

¹ University Hospital Muenster, Germany ² Medical University of Graz, Austria ³ HELIOS Klinikum Emil von Behring, Berlin ⁴ HELIOS Klinikum Bad Saarow ⁵ Medical University of Graz ⁶ HELIOS Klinikum Berlin-Buch, Germany

Background: Little is known about the metastatic potential of low-grade chondrosarcoma. The objective of this study was to evaluate the rate of distant metastasis and attempt to identify possible risk factors.

Methods: The files of 211 patients with newly diagnosed, low-grade chondrosarcoma of bone treated between 1976 and 2010 were retrospectively analyzed. Mean follow-up was 99 months for survivors (range, 24-424 months). 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: Distant metastases developed in 15 patients after a mean of 56 months (range, 4-125 months). 7 of these patients have died of disease, 6 are alive with disease and 2 patients are in complete remission. Post-metastasis survival amounted to 63% after 2 years and 35% after 5 years. 12 of the 15 patients developed local recurrences prior to metastatic disease, 8 of which were grade II. Regarding risk factors, patients with metastases had a mean tumor size at diagnosis of 7.9cm, compared to 8.7cm for patients who did not develop metastases ($p=0.947$). Patients with tumors of the thoracic wall had a significantly lower 10-year metastasis-free survival of 55%, compared to patients with tumors of the upper extremity (98%, $p=0.003$), the lower extremity (91%, $p=0.028$) and the pelvis (90%, $p=0.036$). There were no significant differences in metastasis-free survival between patients treated with intralesional curettage compared to those treated with wide resection ($p=0.711$). Patients who developed local recurrences had a significantly poorer 10-year metastasis-free survival, compared to patients who developed no local recurrences (64% vs. 96%, $p<0.001$). Patients with low-grade local recurrences had a strong trend for a higher metastasis-free survival compared to patients with grade II recurrences (80% vs. 49% at 10 years, $p=0.062$).

Conclusion: Tumor localization in the thoracic wall and development of local recurrences were associated with a higher metastasis rate in this study, while tumor size and surgical treatment modality were not. Given the rarity of grade I chondrosarcoma and its low metastasis rate, further analysis of the risk of metastasis in these patients can only be achieved through large multi-institutional studies.

E-mail (main author): dimosthenis.andreou@ukmuenster.de



O6:103

How safe is curettage of low-grade cartilaginous neoplasms following radiological diagnosis alone?

Matthew Brown¹, PD Gikas¹, JS Bhamra¹, JA Skinner¹, WJS Aston¹, RC Pollock¹, A Saifuddin¹, TWR Briggs¹

¹Royal National Orthopaedic Hospital, United Kingdom

Background: Low-grade chondrosarcomas are managed with intralesional curettage +/- adjuvant measures. Pre-operative differentiation between enchondromas, low-grade chondrosarcomas and high-grade chondrosarcomas remains a diagnostic challenge.

Aim: To ascertain the accuracy and safety of radiological grading of cartilaginous neoplasms through assessment of, (1) pre-operative radiological and post-operative histological concordance and, (2) recurrence in lesions confirmed as high-grade on surgical histology.

Method: A retrospective review of cartilaginous neoplasms managed as low-grade between 2001 and 2012 was completed at our Sarcoma Unit. Pre-operative diagnoses resulted from multi-disciplinary consensus solely following radiological review.

Results: Fifty-five patients were reviewed [mean age 47.3 years (8 - 71); 24 males, 31 females]. Neoplasms involved the femur (n=21), humerus (n=18), tibia (n=9), fibula (n=3), radius (n=3) and ulna (n=1). Surgical histology confirmed 2 enchondromas, 51 low-grade chondrosarcomas and 2 high-grade chondrosarcomas (located in the femur and tibia). A single grade 2 case underwent revision with tibial diaphyseal replacement. Three low-grade patients developed local recurrence [mean 15 months (12 - 17)], with two recurring once and one recurring twice. All recurrences were curetted. No high-grade cases, having demonstrated low-grade disease on pre-operative investigations, developed local recurrence or metastasis [mean 4.1 years (3.3 and 4.9 years)].

Conclusion: Cartilaginous neoplasms identified as low-grade on pre-operative imaging should be managed as low-grade without the need for pre-operative histology. A small proportion of these cases may demonstrate high-grade features on surgical histology but this does not appear to affect recurrence rates. Neoplasms demonstrating borderline high-grade radiographic features should be considered for pre-operative biopsy.

E-mail (main author): matthew.brown@doctors.org.uk



O6:104

LONG-TERM OUTCOME IN 64 PATIENTS AFTER CURETTAGE WITH POLYMETHYLMETHACRYLATE FOR GIANT CELL TUMOR AROUND THE KNEE: HIGHER RISK OF OSTEOARTHRITIS?

Lizz van der Heijden¹, A.C. Heineken², M. Fiocco³, R.G.H.H. Nelissen², M.A.J. van de Sande², P.D.S. Dijkstra²

¹ Leiden University Medical Center ² Orthopedic Surgery, LUMC, Leiden ³ Medical statistics&bio-informatics, LUMC, Netherlands

BACKGROUND Standard treatment for giant cell tumors (GCT) is curettage with polymethylmethacrylate (PMMA). It has been hypothesized that hyperthermic reactions and rigid elasticity of PMMA in the subchondral area may increase the risk for degenerative changes, but a clear definition or evaluation system has not been presented. Study goals were the determination of prevalence, risk factors and clinical relevance of radiological osteoarthritis after curettage with PMMA for GCT around the knee.

METHODS In this retrospective single-center study, we included 64 patients (from 78) with GCT around the knee treated with curettage and PMMA (1987-2010). Radiological osteoarthritis was defined as Kellgren&Lawrence-grade (KL) 3-4. We determined influence of age, gender, tumor-cartilage distance, subchondral bone involvement, intra-articular fracture and number of curettages on KL3-4 progression. SF-36, MSTs and KOOS were obtained to assess functional outcome and quality of life.

RESULTS Median age at final follow-up was 42 years (19-70). There were 34 males. At a median follow-up of 79 months (24-286), eight patients (12%) had progression to KL3, two (3%) to KL4 and one had preexistent KL4 (Table 1). No patient underwent surgery for clinical osteoarthritis. Multivariate Cox regression demonstrated increased hazards of KL3-4 progression when more subchondral bone was affected (hazard ratio=5.7; 95%CI=1.1-31; p=0.042) (Figure 1). In univariate Cox regression, this risk was most apparent when >70% was affected (HR=4.7; 95%CI=1.2-18; p=0.0026) and was also increased when tumor-cartilage distance was <1mm (HR=9.4; 95%CI=1.1-82; p=0.042). Age, gender, intra-articular fracture and number of curettages did not influence KL3-4 progression. Patients with KL3-4 reported lower KOOS symptoms (62vs.82; p=0.022), but scores were similar for pain, daily activities, sports/recreation and quality of life as well as MSTs (22vs.24) and SF-36 (77vs.80) (Figure 2).

CONCLUSION 15% of patients with GCT around the knee had progression to radiological osteoarthritis (KL3-4), compared with 0.3-1.8% in the general population. No lesser function or quality of life was reported and no patient required surgery for clinical osteoarthritis, supporting the assumption that clinical relevance of radiological osteoarthritis after curettage with PMMA may be questioned. Curettage with PMMA is a good treatment option, even in the presence of risk factors for radiological osteoarthritis.

E-mail (main author): l.van_der_heijden@lumc.nl



O6:105

GIANT CELL TUMORS OF THE SMALL BONES OF HANDS AND FEET: LONGTERM RESULTS OF 30 PATIENTS AND LITERATURE REVIEW

Lizz van der Heijden¹, V.C. Oliveira², I.C.M. van der Geest³, D.A. Campanacci⁴, C.L.M.H. Gibbons⁵, M.A.J. van de Sande⁶, P.D.S. Dijkstra⁶

¹ Leiden University Medical Center, Netherlands ² Orthopedic Surgery, CHP, Porto, Portugal ³ Orthopedic Surgery, UMCN, Nijmegen, Netherlands ⁴ Orthopedic Oncology, AOUC, Florence, Italy ⁵ Oxford Sarcoma Service, NOC, Oxford, United Kingdom ⁶ Orthopedic Surgery, LUMC, Leiden, Netherlands

BACKGROUND Giant cell tumors (GCT) of small bones are rare (5%) and may behave more aggressively than GCT of long bones. Only few case-series are published, mainly single case-reports. Surgical treatment varies widely in literature, with highly variable recurrence-rates (0-100%). Study aims were to perform a systematic literature review and to evaluate outcomes after different surgical techniques.

METHODS First, we included twelve papers (from 775 titles) with more than two patients. Titles, abstracts and full-text papers were reviewed by two reviewers. Average recurrence-rate was 72% (18/25; 0-100%) for curettage, 13% (2/15, 0-50%) for curettage with adjuvants and 15% (6/41; 0-50%) for resection. Second, we retrospectively reviewed 31 patients who underwent surgery for GCT of the small bones in one of five tertiary referral centers for orthopaedic oncology (1987-2010). One patient was excluded because of malignant GCT and we included 30 patients; the largest series on GCT of the small bones so far. Six patients underwent curettage, 18 curettage with phenol or liquid nitrogen, with or without polymethylmethacrylate (PMMA) and six resection. We evaluated recurrence and complication-rates, risk factors and functional outcome.

RESULTS At a median follow-up of 5 years (range 2-22) recurrence-rate was 50% (3/6) after curettage, 22% (4/18) after curettage with adjuvants and 17% (1/6) after resection. Five-years estimated recurrence-free survival (Kaplan-Meier) was 50% for curettage, 75% for curettage with adjuvants and 80% for resection (Log-rank; $p=0.423$). The only complication was pain (1/30) which resolved after surgical removal of PMMA remnants. We could not identify individual factors correlated to higher recurrence or complication risks. Mean Musculoskeletal Tumor Society (MSTS) scores were slightly higher after intralesional treatment (29 (20-30)) and resection (25 (18-30)) ($p=0.091$).

CONCLUSION In this largest series on GCT of the small bones, we report the lowest recurrence-rate for resection, followed by curettage with adjuvants. No risk factors for recurrence or complication were identified. Functional outcome may be impaired after resection but was comparable after all techniques in this series. Repeated curettage with adjuvants finally resulted in cure of all patients and is therefore a feasible treatment option in both primary and recurrent GCT of the small bones.

E-mail (main author): l.van_der_heijden@lumc.nl



O6:106

Hand Tumors - Series of 110 cases

Chetan DM¹, Kaladagi P.S²

¹⁾ MMCRI ²⁾ Dr., India

Introduction:

Hand tumors are usually rare and there is not much literature about series of cases. We have studied a series of 110 cases. Hand tumors do consists of both benign and malignant cases.

Methods:

We studied series of 110 cases at Karnataka Institute of Medical Sciences, Hubli and Mysore Medical College & Research Institute, Mysore.

We retrospectively reviewed the records of 110 patients who underwent double ray amputations at our center over few years: few had amputations of the fourth and fifth rays and others amputation of the second and third rays.

Mean age at surgery was 34 years (range, 10–45 years), and minimum follow up was 64 months (mean, 98 months; range, 64–136 months). Some patients had high-grade soft tissue sarcomas of the hand, synovial sarcomas, malignant peripheral nerve sheath tumors, and undifferentiated sarcoma. No patients had detectable metastases at surgery.

Results

All patients were completely disease-free at latest follow up. One patient was alive with lung metastases detected 32 months after surgery. No patients developed local tumor recurrence. Functional assessment showed a mean Musculoskeletal Tumor Society score of 24 (range, 19–28) and mean grip strength 24% of the contra lateral side (range, 17%–35%).

Conclusions

The majority of osseous tumors of the hand are benign.

Ganglion cyst is the most frequently encountered comprising 50-70% of benign tumors of hand.

Enchondroma was the next common benign bone tumor followed by osteoid osteoma, osteoblastoma, aneurismal bone cyst, giant cell tumor, epidermoid cyst, and osteochondroma.

Malignant tumors of the hand are rare, although there remain many instances in which marginal excisions are performed for unsuspected malignant hand lesions. Suboptimal biopsy incisions and inadvertent contamination during these excisions may result in larger resections or amputations being necessary to ensure complete removal of the tumor with negative margins.

E-mail (main author): chetandm1987@gmail.com



O6:107

Campanacci III giant cell tumour of the knee: curettage versus primary resection

Czar Louie Gaston¹, Jose Albergo², Krishna Reddy¹, Adesegun Abudu¹, Simon Carter¹, Lee Jeys¹, Roger Tillman¹, Robert Grimer¹

¹Royal Orthopaedic Hospital, United Kingdom ²Hospital Italiano de Buenos Aires, Argentina

Background: Giant cell tumours of bone (GCT) are benign aggressive primary bone lesions most commonly seen around the knee (distal femur, proximal tibia). Campanacci grade III tumours have significant bone destruction and expansion into the soft tissues and although detailed curettage is the standard treatment for GCT, some authors recommend outright resection for Campanacci III tumours due to the higher risk of local recurrence. This study looks at the roles of curettage and primary resection of Campanacci III GCT of the knee.

Methods: Retrospective review of 141 patients treated at our institution from 1980 to 2010. Patients were grouped by initial surgical treatment, curettage versus resection. Local recurrence and functional outcomes were the primary endpoints investigated.

Results: Mean follow-up of 63 months (range 3 – 438 months). 73% (n = 103) were treated by detailed curettage with or without cementation while 27% had outright resection. While local recurrence for the curettage group was significantly higher (21.4% vs 5.3% p = 0.002), MSTS scores on final follow-up was lower for those treated with resection (25.1 vs 27.3, p = 0.006). 25% (n = 26) of those initially treated with curettage eventually underwent joint resection because of local recurrence or complications of curettage (osteoarthritis, fracture). Those that underwent secondary resection did not have different functional outcomes than the primary resection group (MSTS score 24.5 vs 25.1 p = 0.31). No local recurrence of GCT was seen after secondary resection.

Conclusions: Detailed curettage with or without cementation has a higher risk for local recurrence but has better functional outcomes than primary resection. Secondary resection due to failed curettage is not associated with poorer functional outcomes or local recurrence.

E-mail (main author): louie.gaston@nhs.net



O6:108

Aneurysmal bone cysts-Does simple treatment work?

Krishna Reddy¹, Louie Gaston¹, Raj Nandra¹, Friedl Sinnaeve², Robert Grimer¹

¹) Royal Orthopaedic Hospital, United Kingdom ²) University Hospital Leuven, Belgium

Background:

Aneurysmal bone cysts (ABC) are benign expansile bone lesions, with an estimated incidence of 1.5/million. Treatments include a variety of procedures including detailed curettage with or without adjuvants. We observed that a number of ABCs will, Üheal, following biopsy alone and as a result of this we changed our treatment regime.

Methods:

All patients with a radiologically presumed ABC had a biopsy to confirm the diagnosis and during the biopsy samples were taken from all areas of the lesion. Following tissue diagnosis patients were reviewed at 6 weeks with new radiographs. If the lesion showed signs of healing and patients reported symptomatic improvement, they were followed up with observation only. If the lesion or symptoms progressed, they underwent definitive treatment with detailed curettage.

Results:

Two hundred consecutive patients, diagnosed with an ABC in our unit from year 2000 to the end of 2011 were included. Eighty-eight of them underwent immediate treatment following biopsy due to the size, symptoms of the lesion and risk of fracture. Hundred and two patients had a biopsy or a curopsy (a technique not described in literature) and were then observed as per the protocol above. Nine patients presented with pathological fractures and had symptomatically improved as the fracture healed. One patient had an incidental asymptomatic lesion. Of the 102 patients who had curopsy or a biopsy, 82 (80%) required no further treatment and the lesion resolved. Twenty patients had no evidence of healing at 6 weeks and underwent definitive curettage. The overall recurrence rate in these 200 patients was 15% whilst in the 88 patients undergoing definitive curettage (with or without adjuvant therapy) it was 10% (9/88).

Conclusion:

This rate of spontaneous healing following curopsy/biopsy alone needs consideration when evaluating the results of any other treatment for ABC, suggesting simple treatment strategies work for ABC.

E-mail (main author): k.reddy@nhs.net



O6:109

Do periprosthetic seromas contribute to a third space effect after high dose Methotrexate?

Claudia Heu¹, Volker Strenger¹, Joanna Szkandera¹, Joerg Friesenbichler¹, Georg Prattes¹, Ernst-Christian Urban¹, Andreas Leithner¹

¹ Medical University of Graz, Austria

BACKGROUND Beside surgery, high dose Methotrexate is a mainstay of osteosarcoma treatment. However, it is associated with severe side effects, which partly are dose dependent. Methotrexate tends to accumulate in tissues and cavities (third spaces) leading to local toxicity and delayed elimination. In order to avoid this, considerable periprosthetic seromas are punctured in our institution, despite an increased risk of infections. The aim of our study was to analyse Methotrexate concentrations in seroma and blood to verify a potential toxic risk based on a third space effect.

METHODS In a monocentric data analysis of 53 consecutive osteosarcoma patients (5 – 46, median 15 years) who had received an endoprosthesis and who were treated with high dose Methotrexate from 1991 till 2011, we retrospectively compared Methotrexate concentrations in seromas with the corresponding (+/- 8 hours) concentrations in blood.

RESULTS 114 periprosthetic seroma punctures were performed in 18 of 53 patients (median 5 punctures per patient, range 1 - 20 punctures per patient). The amount of punctured effusions was documented in 101 punctures, ranging from 5 - 420 ml (median 150 ml). Methotrexate concentrations were determined in 61.1% of all punctures and were 249 – 4397% (median 1586%) of the corresponding blood concentration at 24 hours. 48 and 72 hours Methotrexate concentrations of seromas were 236 – 535% (median 950%) and 166 – 682% (median 366%) of the corresponding blood concentrations, respectively. Especially the 24 hours measurements of the seromas ranged up to highly toxic concentrations of 170.74 µmol/l (median 109.83 µmol/l, range 4.91 - 170.71 µmol/l) in comparison to a median value of 4.65 µmol/l in blood (range 0.68 - 44.38 µmol/l, p=0.001 (Wilcoxon test)). Similar statistically significant differences indicating a third space effect were observed at 48 (p<0.001) and 72 hours (p=0.015).

CONCLUSIONS In conclusion, Methotrexate concentrations of effusions are significantly higher than corresponding blood levels indicating that periprosthetic seromas might act as a third space after high dose Methotrexate, potentially leading to severe local and systemic side effects. These effusions should therefore be punctured in order to avoid increased toxicity.

E-mail (main author): claudia.heu@stud.medunigraz.at



O6:110

Intraoperative extracorporeal irradiation and reimplantation of tibial malignant sarcomas after wide resection

Andreas H Krieg¹, Leandra Schultze², Bernhard Speth², Peter Gross³, Martin Haug³

¹) University Childrens Hospital Basel ²) University Childrens Hospital ³) University Hospital Basel, Switzerland

Background:

Diaphyseal tibial sarcomas are commonly treated with a wide resection and reconstructed with allografts with or without vascularised fibula, with reconstruction over a segmental transport or with the induced membrane technique. This is the first larger series presenting an alternative inexpensive and biological method that to our knowledge has not been reported on before.

Methods:

Eight Patients with primary malignant tibial sarcomas received local treatment in form of reimplantation of extracorporeally irradiated (ECI) autografts after its wide resection. The mean age at the time of diagnosis was 29 years (range 12.2 to 60). Radiation dose for the tibial segment was 50 Gy in all cases. ECI was combined with an ipsilateral vascularised fibula (n = 5) in those cases where a partial bone stock of the tibia could not be preserved. The functional results were expressed as the Musculoskeletal Tumor Society score (MTS) and the Toronto extremity salvage score (TESS). The mean clinical and radiological follow-up was 40 months (range, 12 to 66).

Results:

All patients had clear margins after the performed wide resection and were free of disease and without evidence for local recurrence at the time of the last follow up. There were postoperative complications in 3 patients. Full weight bearing was allowed at the time of radiological consolidation of the irradiated graft which was achieved after a mean of 6 months (range 3 to 12). The vascularised fibula autografts showed a significant hypertrophy in 8 of 10 junctions. The functional results were good and excellent in 7 of 8 patients in the MTS-Score and Toronto extremity salvage score.

Conclusion:

We conclude that ECI grafting, also in combination with vascularised fibula in large defects, is a suitable method for the treatment for localised and resectable tibial sarcomas with good to excellent functional results.

E-mail (main author): andreas.krieg@ukbb.ch



07:101

"The Classics"

Björn Gunterberg¹

¹ Sahlgrenska University Hospital, Sweden

Bertil Stener made Gothenburg one of the cradles of musculoskeletal tumor surgery when he already in the 1960's developed a profound interest in this area. He was a pioneer and the father of many classical works in different fields of musculoskeletal tumor surgery.

I will focus on his ingenious approaches to tumors of the spine and sacrum with special emphasis on his spinal reconstructions. Those four patients who had had total spondylectomy

and the longest follow-up will be presented in detail. Lasting, stable reconstruction of the spine was achieved with autologous bone grafts and "primitive" supporting metallic implants (AO-plates, wires, screws, Meurig-Williams plates, Harrington rods, Dwyer compression wires). Because of the questionable strength of the implants and their anchorage to the spine the patients were kept in bed rest for 2-6 months and wore plaster jackets for 8-12 months.

The long-term results (23-44 years) are extremely good. MSTS-scores ranged from 70-87 per cent. Stener's reconstructions of the spine have stood the test of time.

Also his principles and method for high amputation of the sacrum were based on analytical skill, profound knowledge and surgical ability. They are still adhered to.

Classical works will always be remembered.

E-mail (main author): bjorn.gunterberg@telia.com



07:102

Video laparoscopic approach – Technique for sacral resection

Eduardo Sadao Yonamine¹, Élio Consentino¹, Paulo Augusto Ayrosa Galvão¹, Pedro Péricles Ribeiro Baptista¹, José Donato Próspero¹, Maria Fernanda Carriel Amary¹, Karen Voltan¹, Felipe Birriel¹, Bruna Bruscharino¹

¹ Santa Casa Medical School of Sao Paulo, Brazil

OBJECTIVES

Present our long term follow up after huge sacral tumor resection without reconstruction in the last 10 years we performed resection of huge sacral tumors in two steps, first anterior approach by videolaparoscopy to tie and isolated iliac vessels and posterior open approach to resection the tumor.

METHODS

From January 1990 to July 2010, we treated 74 patients with Primary Sacral Tumor in Santa Casa Medical School of Sao Paulo (Brazil) We exclude all cases treated exclusively by radiation therapy, metastatic lesions, multiple myeloma and lesions that doesn't need anterior and posterior approach. Considering 20 cases with huge primary bone tumor that need anterior and posterior approach to resect the lesion and performed the anterior approach by Videolaparoscopy.

RESULTS

We analyse all 20 cases with primary bone tumor and follow up from 38 to 312 months (average of 185 months). Epidemiology: All 20 cases diagnosis: 8 (40,0%) Chordoma, 7 (35,0%) Giant Cell Tumor, 2 (10,0%) Ewing's Sarcoma, 2 (10,0%) Chondrosarcoma and 1 (5,0%) Osteosarcoma. Complications: 4 post operative infections 1 necrosis and colostomy 1 temporary colostomy 1 local recurrence.

CONCLUSIONS

We considering anterior approach by videolaparoscopy safe and save time for Sacral Resection and give satisfactory function for our patients.

E-mail (main author): esy.pfs@gmail.com



07:103

Endoscope assisted total spondylectomy for malignant or aggressive bone tumors of the spine

Yong-Koo Kang¹

¹ St. Vincent's Hospital, Republic Of Korea

Introduction: Primary malignant and aggressive bone tumors of the spine are very rare. Early diagnosis and complete removal of the tumor are essential for prevention of local recurrence and metastasis.

Purposes of the study are to show the local recurrence and final results of total spondylectomy for malignant or aggressive spinal tumors with endoscope assisted versus conventional anterior and/or posterior approaches

Materials and Methods: From 1996 to 2012, total 29 patients with malignant or aggressive bone tumors of the spine had been surgically treated and followed for minimum a year to 15 years. Diagnoses were 10 giant cell tumors, 5 chordomas, 4 malignant lymphomas, 2 osteosarcomas, 2 chondrosarcomas, 2 MPNST, 1 Ewing's sarcoma, and 1 hemangioendothelioma and 2 metastatic cancers (1 breast, 1 cervix). All patients had been treated with total spondylectomy with anterior and/or posterior approaches. Six of them had been treated with the endoscope (2 thoracoscope, 4 laparoscope) assisted total spondylectomy. Anterior dissection was done with thoracoscope for dorsal spine, and laparoscope for lumbar and sacral spines. After surgical removal of the vertebral body, metallic cage with bone graft, strut allograft or autograft were placed, and anterior and posterior stabilization procedures were performed.

Results; Among 17 patients of primary malignant tumor, 7 were died of disease, 4 alive with disease and 6 continuous disease free. Among 10 giant cell tumors, 3 local recurrences developed. There were 1 (17%) local recurrences from 6 patients of endoscope assisted total spondylectomy and 9 (39%) recurrences from 23 patients of conventional spondylectomy.

Conclusion: Total spondylectomy with anterior and/or posterior approaches was essential to reduce local recurrence and long term clinical results for malignant or aggressive spinal tumors. Endoscope assisted surgery has been reduced the total spondylectomy related morbidity and complications.

E-mail (main author): ykang@cmcnu.or.kr



O7:104

Outcome of Surgical Treatment of Pelvic

Wei Guo¹, Xin Sun¹, Tao Ji¹, Xiaodong Tang¹

¹ Peking University People's Hospital, China

Methods: 22 consecutive patients with pelvic osteosarcoma underwent surgical procedures between June 2000 and June 2009. There were 13 males and 9 females with a mean age of 29.7 years. According to Enneking and Dunham pelvic classification system, there were 3 cases with Type I, 3 cases with Type I+IV, 5 cases with Type I+II, 4 cases with Type II+III, 1 case with Type I+II+III, 1 case with Type III, and 5 cases with type I+II+IV. Twenty-one of 22 patients were diagnosed pathologically as the conventional and the other one was low-grade osteosarcoma. All the patients received en bloc resections including 17 wide or marginal margins and 5 intralesional margins. Fourteen patients underwent modular hemipelvic endoprosthesis reconstruction and 6 patients underwent rod-screw system reconstruction combined with autograft, and 2 patients with no reconstruction after resection. The mean follow-up time was 30.3 months (ranged from 4 to 89).

Results: Local recurrence rate was 31.8% (7/22), including 4 of 5 patients with intralesional margins, 3 of 16 with wide or marginal margin. The local recurrence rate was 17.6% (3/17) in patients with wide or marginal resections, and 80% in patients with intralesional surgery (4/5). At the last follow-up, lung metastasis was found in 9 of 22 (40.9%) patients, and bone metastasis was found in one patient.

Among 22 patients with pelvic osteosarcoma, 8 patients died, 5 patients alive with diseases and other 9 patients with tumor-free survive. The 5-year overall survival rate was 44.3%. The average MSTS 93 score was 17.6 ± 5.4 for the 14 patients with hemipelvic endoprosthetic reconstruction and 22.5 ± 2.1 for 6 patients with rod-screw reconstruction. Wound complication was found in 7 of 22 patients (31.8%).

Conclusion: The majority of the patients with pelvic osteosarcoma can be treated with limb salvage surgery and can be preserved good function after the surgery. The long-term oncological result is still not satisfied because of anatomic location, big volume of the tumor at the surgery. Five years survival is much lower than that in osteosarcoma of the extremity.

E-mail (main author): bonetumor@163.com



O7:105

Surgical Tumor Resection in Combination with Pre-Operative Radiation for Treatment of Primary Sacral and Coccygeal Chordomas

Polina Osler¹, Kathryn Hess², Ying-Ling Chen², Thomas DeLaney², Al Ferreira², Kevin Raskin², Joseph Schwab², Francis Hornicek²

¹Harvard Medical School ²Massachusetts General Hospital, United States

BACKGROUND:

A combination of pre-operative radiation and surgical resection has been proposed as an alternative to surgical resection alone to reduce the rate of tumor recurrence in spine chordoma patients. To evaluate the efficacy of this treatment regimen, we conducted a retrospective cohort study of the primary sacral and coccygeal chordoma patients, who were treated at the Massachusetts General Hospital during 1999-2011.

METHODS:

38 patients treated with pre-operative radiation (20-50 Gy) and surgery for primary sacral (34) or coccygeal (4) chordoma were followed for an average of 58 months. Patients were retrospectively assigned into two groups based on the status of surgical resection margin: negative or microscopically positive. Radiographic evidence was used to evaluate the local disease recurrence status and/or presence of metastatic disease. We used Kaplan-Meier survival analysis with LogRank significance test to analyze disease-free survival in each group. Stratified Cox model was used to look for significant confounders.

RESULTS:

There were 6 deaths recorded in the series (16%); 2 were attributable to disease, and 4 to other causes. The mean overall survival time was 75 months. The mean disease-free survival was 102 months. 6 patients in the series developed metastatic disease (16%). Of those, 2 died of disease and 4 were alive with disease at the time of last follow-up in 2012 (average follow-up time was 15 months). None of the 38 patients in the series had a local disease recurrence after en bloc resection. The final surgical pathology results were available for 35 of the 38 patients. Tumor resection margin was negative in 32 patients, with 6 metastases in this group. Margins were reported positive in 3 patients. The average follow-up time in the group with positive resection margins was 91 months (range 61-138 months), with no disease-specific deaths recorded during this time. Patient age at the time of surgery was found to be a statistically significant confounding variable, with advanced age corresponding to lower post-operative survival.

CONCLUSION:

Our results indicate that en bloc resection of the primary tumor in combination with pre-operative radiation was associated with good overall and disease-free survival, and no local recurrences.

E-mail (main author): posler@partners.org



O7:106

En Bloc Resection in Combination with High Dose Radiation Improves Patient Survival in Mobile Spine Chordoma

Polina Osler¹, Kathryn Hess², Thomas DeLaney², Kevin Raskin², Ying-Ling Chen², Al Ferreira², Francis Hornicek², Joseph Schwab²

¹ Harvard Medical School ² Massachusetts General Hospital, United States

BACKGROUND:

Surgical resection of the primary tumor is the mainstay treatment for chordoma of the mobile spine. However, control of local disease recurrence remains poor. Aggressive tumor resection in combination with high dose proton beam radiation has been proposed at our institution to improve disease-free survival by reducing recurrence rates. To evaluate the effect of this therapy, we conducted a retrospective study of 49 patients with chordoma, who were treated with combination high-dose radiation and surgical resection at the Massachusetts General Hospital during 1992-2013.

METHODS:

49 patients who received surgery and high dose radiation (>70 Gy) were retrospectively assigned into two groups based on extent of resection. 15 patients had en bloc resection; mean age was 48 years old, mean follow-up time was 42 months. 34 patients had intralesional resection; mean age was 57 years old, mean follow-up time was 63 months. We documented resection margin pathology, disease recurrence, and/or presence of metastases. We used Kaplan-Meier analysis with LogRank significance test to calculate overall survival and disease-free survival. Recurrence rates were compared using two-tailed Wilcoxon rank sum test. Stratified Cox model was used to identify confounding factors.

RESULTS:

Of the 49 patients in the series, 15 developed recurrent disease and 7 developed metastases. 15 patients had en bloc resection; 2 developed recurrent disease, and 2 developed metastases. Margins were negative in 6 patients; there were no mets or recurrences. 34 patients had intralesional resection; 13 developed recurrent disease, and 5 developed metastases. The mean overall survival was 108 ± 14 months; and 107 ± 16 months in the intralesional group. There were no deaths in the en bloc group. En bloc resection was associated with improved disease-free survival (P = 0.033) and overall survival (P = 0.020), but not the local recurrence (P = 0.588). Margin status did not significantly influence disease-free survival (P = 0.100) or rate of recurrence (P = 0.089).

CONCLUSION:

En bloc resection in combination with high dose radiation significantly improved disease-free survival and overall survival in our series. The frequency of local disease recurrence was 30.6% despite positive resection margins, possibly attributable to high dose radiation therapy.

E-mail (main author): posler@partners.org



O7:107

Surgical resection of sacral chordoma: an update of the Rizzoli experience on 71 cases.

Pietro Ruggieri¹, Andrea Angelini¹, Gabriele Drago¹, Giulia Trovarelli¹, Fernando Jorge¹, Carlo Romagnoli¹, Andrea Ferraro¹

¹ University of Bologna, Istituto Rizzoli, Italy

Background. The treatment of choice in sacral chordoma is surgical resection. Wide margins obtained at initial surgery are the primary factor to improve survival. Our aim was to analyze the outcome in a large series of patients with sacrococcygeal chordoma at long-term followup, in order to help to define the role of previous inadequate surgery, surgical margins and the relationship with local recurrences.

Methods. We retrospectively reviewed 71 patients with sacral chordomas treated with surgical resection. Forty-eight resections were proximal to S3, 23 below or at S3. Proximal resections required an anterior and posterior approach with the exception of the 8 patients treated with a new technique using a posterior approach only, as well as 3 cases of distal resection. Eleven received previous intralesional surgery elsewhere. Three reconstructions were performed.

Results. Margins were wide in 44 resections, wide but contaminated in 11, marginal in 9 and intralesional in 7. Patients previously treated had wide margins in 7 cases, wide but contaminated in 2, marginal and intralesional in one each. Three patients died for postoperative complications and were excluded from further analysis. Overall survival was 92%, 65% and 44% at 5, 10 and 15 years respectively. At a mean follow-up of 9.5 years (min 0.5, max 32 yrs) 37 are NED (54.4%): 27 continuously NED, 5 NED1, 1 NED2, 4 died of different disease. Twenty-three died with disease (33.8%) and 8 are alive with disease (11.7%). Relapses included 15 local recurrences, 6 distant metastases, 17 both. Local recurrence rate was strictly related with margins.

Local recurrence rate was significantly higher in patients that received previous intralesional surgery ($p=0.0217$). Factors that influence local recurrence rate were margins other than wide ($p=0.0339$) and tumor volume at different cut-offs ($p<0.01$), whereas level of resection was not significant ($p=0.5883$). Multivariate analysis confirmed the role of tumor volume. Complication rate was high (80.9%) with an infection rate of 41.2%.

Conclusion. The most prominent adverse factor for local recurrence was previous intralesional surgery. Local recurrence rate was related with inadequate margins and tumor volume. Oncologic outcome of major resections is comparable to minor.

E-mail (main author): pietro.ruggieri@ior.it



O7:108

Ewing sarcoma of the sacrum: clinical outcome of 19 patients in a single institution

Pietro Ruggieri¹, Xin Sun¹, Gabriele Drago¹, Andrea Angelini¹, Carlo Romagnoli¹, Marco Maraldi¹, Mohammad Hassani¹

¹ University of Bologna, Istituto Rizzoli, Italy

Background:

Ewing's sarcoma occurs rarely in the sacrum with incidence of 1-2%. Although overall results of treatment of Ewing's sarcoma have improved with multimodal strategies, unfortunately, in the sacrum it has worse prognosis than in other sites. A retrospective analysis describes our experience with respect to oncological outcome and neurologic function

Methods: We retrospectively reviewed 19 patients with Ewing's sarcoma of the sacrum treated between September 1980 and December 2011. Pain and neurologic impairment were the most common symptoms. The mean duration of symptoms was 7.8 months. Three patients received surgery with or without radiation and chemotherapy. One patient had radiotherapy alone. Chemotherapy was given to 18 patients, in 10 of them followed by radiation.

Results:

The mean follow-up was 7,26 years (range 6 months-27 years). In 2 cases we performed surgery, both of them developed local recurrence. Seven patients had metastases at diagnosis while other 5 patients developed metastases during follow up. Overall 13 patients died at mean of 4,72 during the follow-up. The 5-year overall survival (OS) and the 5-year event-free survival (EFS) were respectively 47,3% and 31,5%. Gender and age did not appear to influence OS or EFS statistically.

Conclusions:

The outcome of Ewing's sarcoma of the sacrum was unrelated to gender, age, metastasis at diagnosis and local treatment strategy. Our experience showed that although multimodal treatment could improve the overall survival, Ewing's sarcoma of the sacrum had a significantly worse outcome than in other primary locations

E-mail (main author): pietro.ruggieri@ior.it



O7:109

Chondrosarcoma of the mobile spine and sacrum. A clinical series with minimum 13,5 years follow-up.

Björn Gunterberg¹, Peter Bergh¹, Örjan Berlin¹

¹ Sahlgrenska University Hospital, Sweden

Background: Surgery is the primary option for treatment of chondrosarcoma. There is presently no strong evidence for the benefit of other treatments. The anatomical characteristics of the axial skeleton present difficult surgical problems in the treatment of chondrosarcoma located to the spine and sacrum. We retrospectively investigated the results of our surgical treatment of these tumors with long-term follow-up.

Patients and methods: Nineteen consecutive patients with a minimum observed follow-up of 13,5 years were reviewed. Fourteen were male, 5 female. The mean age at first surgery was 40 years. Twelve patients had tumors of the mobile spine, 7 of the sacrum. The mean tumor size was 11 cm. Tumor grades were: grade I 1, grade II 10, grade III 6 and grade IV 2 patients.

Results: Local recurrence occurred in 37 percent of the patients, metastases in 21 percent. The 5-year survival was 78 percent and 10-year survival 73 percent. The mean overall survival was 15 years (range 1,5-28,5 years). Nine patients had a tumorrelated death and 1 died with disease. Eight patients are alive with a minimum of 13,5 years tumorfree follow-up and 1 patient died of other causes 23,5 years postoperatively. Only one of the patients received radiotherapy. Out of these 9 (47 percent) cured patients 7 had spinal tumors, 2 sacral. Tumor grades were 7 grade II, 2 grade III.

Conclusions: Centralized treatment and aggressive surgical techniques may control approximately 50 percent of chondrosarcomas of the axial skeleton. Local recurrences and metastases are compatible with long survival.

E-mail (main author): bjorn.gunterberg@telia.com



07:110

Results of surgical treatment of Ewing's sarcoma of the pelvis.

Philipp Funovics¹, Madelaine Willegger¹, Stephan Puchner¹, Joannis Panotopoulos¹, Reinhard Windhager¹

¹ Medical University of Vienna, Austria

Aim of this study was to report our single-center experience with surgical resection of pelvic Ewing's sarcoma within a multimodality treatment approach.

Out of the Vienna Bone and Soft Tissue Tumor Registry we have identified 48 patients (25 females and 23 males) with a Ewing's sarcoma of the pelvic or sacral region treated between 1973 and 2012. Mean age at time of surgery was 19 years (median, 17; range 2-51). All but 3 sacral tumors and 3 gluteal soft tissue lesions occurred in the bony pelvic ring. After resection, surgery comprised additional reconstruction by endoprotheses in 15 patients and by biological means in 13 patients. Adjuvant treatment included chemotherapy in 46 patients, radiation in 32 and 31 patients received both. Overall mean follow-up was 54 months (median, 37; range 1-245).

Surgical complications occurred in 19 patients including infection in 7, mechanical disorders in 5, neurological deficits in 4 and thrombo-embolism in 3, one of them ended lethal. Three patients had to undergo secondary hemipelvectomy. Local tumor recurrence appeared in five patients, but all of them were observed before 1985. Nine patients presented with primary metastatic disease, 17 patients developed metastases throughout follow-up. Altogether, 26 patients died of disease, resulting in a median overall survival of 45 months. The respective 5-year overall survival was 42%.

The surgical treatment of pelvic Ewing's sarcoma remains challenging with a relatively high complication rate and moderate overall outcome, local tumor control rates are highly satisfying given an aggressive surgical approach.

E-mail (main author): philipp.funovics@meduniwien.ac.at



07:111

Surgical Outcome of Internal and External Hemipelvectomy in Patients above the Age of 65 years

Wiebke Guder¹, Jendrik Harges¹, Georg Gosheger¹, Marcel-Philipp Henrichs¹, Dimosthenis Andreou¹, Sebastian Bockholt¹, Arne Streitbueger¹

¹) University Hospital Muenster, Germany

Background: Hemipelvectomy is a common treatment for primary malignant tumors of the pelvis. Due to a close proximity to internal organs and major vessels intraoperative complications can be severe. In the post surgical interval complications like infection, vascular occlusion or secondary hemorrhage can occur. Little is known of the surgical outcome in elderly patients who often have comorbidities as an aggravating factor.

Methods: We did a retrospective analysis of the surgical outcome of 37 performed hemipelvectomies in 34 patients of 65 years or older (ranging from 65 - 83 years, mean 70,6 years) at the time of surgery between 1999 and 2012. Data on tumor grading, primary versus recurrent disease, indication for and type of surgical procedure, duration of surgery, perioperative complications, resection margins, duration of stay, stage of disease at the time of surgery, primary and follow-up starting after hemipelvectomy were evaluated.

Results: Of 37 hemipelvectomies an internal hemipelvectomy was performed as primary surgery in 13 patients. 24 patients underwent external hemipelvectomy (as primary surgery in 9, in locally recurrent tumor in 9, in not manageable infection after internal hemipelvectomy in 3 and after intralesional surgery in 3 patients). Mean duration of surgery was 190 minutes (internal 313 min, external 197 min). Mean hospital stay was 54 days for external, 76 days for internal and 116 days for conversion of internal to external hemipelvectomy. Blood-loss differed greatly in between surgeries with a mean transfusion of 10 erythrocyte and 8 fresh frozen plasma banked blood products per surgery. Intraoperative complications were injury of the urethra in 3 patients and one epidural bleeding occurred. Of 21 patients with wound healing complications, 18 patients needed additional surgical approaches (mean of 2,5 surgical revisions/patient). 2 patients died during hospital stay. The mean follow-up was 47 months.

Conclusion: Internal and external hemipelvectomies in patients above the age of 65 years are surgically possible. But depending on a curative or palliative regimen, indications for major surgery have to be strictly evaluated.

E-mail (main author): wiebke.guder@ukmuenster.de



07:112

Quality of Life after Sacral Tumor Resection

Kathryn Hess¹, Polina Osler, MS¹, Yen-Lin Chen MD², Thomas DeLaney, MD¹, Al Ferreira R.N.², Kevin Raskin, MD¹, Dempsey Springfield, MD¹, Francis Hornicek, MD, PhD¹, Joseph Schwab, MD, MS¹

¹) Massachusetts General Hospital ²), United States

Background: En bloc resection remains the treatment of choice for most primary malignant tumors of the sacrum. However, the quality of life following resection of the sacrum is not well-documented in the literature. With the emergence of numerous validated Health-Related Quality of Life survey tools, the study of sacrectomies can be expanded to include the post-operative quality of life for patients.

Methods: Sacral tumor patients of the Stephen L. Harris Center for Chordoma Care were mailed surveys to complete post-operatively addressing general health, pain, bowel function, bladder function, and sexual function. The survey responses were collected and scaled on a scale from 0-100% of the best possible score, where 100% is the highest score available for a patient to indicate favorable quality of life.

Results: A total of 24 patients (13 males, 11 females, average age of 57 years and an age range of 29-76) seen at the Stephen L. Harris Center for Chordoma Care, who have been previously treated surgically with a coronal resection for a sacral tumor were included in the analysis. We collected data on the level of coronal resection cut for each patient. The HRQL scores, which were compiled for each patient-reported outcome category, showed to varying degrees a decrease in the quality of life with the increase in the number of levels involved in the resection. The linear regression for general health and pain, showed the best linear correlations.

Conclusions: Because of the limited number of patients in our data set our conclusions cannot be state with statistical significance, yet general trends can be elucidated from the data. HRQL for each of the categories general health, pain intensity and interference, bowel function, bladder function, and sexual function decreased as the levels involved in the coronal resection increased. The general trend is similar to that inferred from the accepted literature where higher sacral level involvement is associated with a decrease in patient functional outcomes. The most prominent limitation of this study is the small sample size, though data continues to be collected to improve the trend analysis.

E-mail (main author): khess2@partners.org



07:113

Ewing's Sarcoma of the Pelvic Girdle Treated with Cryoablation in Lieu of Wide Local Resection. Report of Eight Consecutive Patients.

Shlomo Dadia¹, Yair Gortzak², Suzy Ben-Eliyahu², Yehuda Kollender², Jacob Bickels²

¹) Tel-Aviv Sourasky Medical Center ²) National Unit of Orthopedic Oncology, Israel

Background

Wide resection of Ewing's sarcoma of the sacrum or periacetabular region may result in a major neurological deficit or loss of hip function and ambulation ability, respectively. The authors speculated that intralesional tumor resection with adjuvant cryoablation of the tumor cavity in lieu of wide local resection may be safely performed in patients who had Ewing's sarcoma of the pelvic girdle and in which the tumor was confined to the affected bone.

Methods

Between 2004 and 2010 the authors treated 6 patients with sacral and 2 patients with periacetabular Ewing's sarcoma. There were 5 males and 3 females who ranged in age from 10 to 41. Five patients had a stage IIA and 3 patients had a stage IIIA disease. All patients were treated with preoperative chemotherapy and following recovery from surgery, chemotherapy and radiation therapy. Surgery included intralesional tumor removal and cryoablation of the remaining tumor cavity. Patients were followed from 1 to 6.5 years.

Results

At their most recent follow-up, none of the study patients had local tumor recurrence. All patients were ambulating without assisting devices and none had neurological deficits that were attributed to the surgical procedure. One patients who had sacral disease developed radiation-induced osteosarcoma of the sacrum.

Conclusions

Intralesional tumor removal with adjuvant cryoablation in patients who have pelvic Ewing's sarcoma and in which the disease has no soft-tissue extension, provide good local control and preserve function. It should be considered as the surgical treatment of choice in these patients.

E-mail (main author): jbickels@012.net.il



07:114

Neurogenic tumors of the sacrum. 10 years experience of a single institution

Elmar Musaev¹, Denis Sofronov¹, Eugeny Sushentsov¹, Kirill Borzov¹, Anastasia Nered¹, Igor Komarov¹, Mamed Aliev¹

¹ N.N.Blokhin RONC, Russian Federation

Introduction: According to various authors, presacral and sacral tumors account less than 5-7% of all spinal tumors. Slow growth and non-specific symptoms often do not allow for timely diagnosis of the disease.

Methods: From 2002 to 2012, 62 patients were operated with paravertebral and presacral neurogenic tumors. The study included 21 patients with lesions of the sacrum. Men-5 and 16 were women. The patients' ages ranged from 22 to 69 years, mean age 39 years. Benign tumors were observed in 17 (81%) patients, malignant 4 (19%). Schwannoma verified in 15 (71.5%) cases, neurofibroma 4 (19%), ganglioneuroma 2 (9.5%). Before surgery, all patients evaluated by Karnofsky, Frankel, Klimo scales. Pain syndrome was estimated on VAS and Watkins scale. The first step was sacral laminectomy with resection or root sparing microsurgery and the posterior mobilization of the tumor. The second stage included anterior endoscopic or open approach in cases of large intrapelvic component, for remove presacral tumor component.

Results: 21 operations were performed. Two patients underwent surgery treatment from the posterior approach, three ones with anterior and 16 with combined approach. In 8 cases the operation was performed with endoscopic stage. Follow-up was 3 to 120 months; the median time was 55 months. 2 patients died. One as a result of the progression of the underlying disease (malignant schwannoma G3, associated with neurofibromatosis type 1), and one because of early postoperative complications (wound infection, meningitis). Recurrence was observed in two cases of malignant shwannomas what were associated with nonradical surgical treatment and large tumor size. In one case after endoscopic removing of presacral tumor developed bleeding that required urgent revision surgery.

Conclusions: Surgical treatment of patients with neurogenic tumors involves the sacrum gives good functional and oncological outcome. High-grade tumors in combination with neurofibromatosis have a worse prognosis as the most of the high risk of relapse, and life expectancy. The use of two stage surgical treatment increased the possibilities of radical operation in patients with the tumor of sacrum. Using of the endoscopic technique allows decreasing a blood loss, wound complications, and improving a cosmetic effect and rehabilitation.

E-mail (main author): nisichenko@gmail.com

**MGL2:101**

Teamwork in Musculoskeletal Oncology

*Franklin H. Sim¹**¹⁾ Mayo Clinic, United States*

The speciality of musculoskeletal oncology is very compelling and supports the value in reflecting on recent developments in the field including the challenges and problems encountered in order to meet the demands of a new era.

Currently efforts continue towards improving local control of the tumor while retaining function in the reconstructive limb. The major challenges include defining the adequacy of surgical margins and secondly developing biological and prosthetic reconstructions to match the improved life expectancy. Close collaboration between clinical practice, basic science, and bioengineering has expanded the range of biological and nonbiological methods to maximize function. The wealth of knowledge gleaned from physics, engineering, and metallurgy has been used to improve the manufacture and design of prosthesis. Efforts continue to develop techniques to maximize function and make the reconstruction more durable.

Much of the progress in this field is due to teamwork. From the historical perspective, the evolution of the specialty of musculoskeletal oncology has been enhanced by teamwork; all the disciplines working together to advance the science and make a real difference in the lives of our patients.

One of the most important areas where a team approach is indicated to enhance the success in achieving clear margins and to improve function is in tumors of the pelvis and sacrum. The specialization of our surgical practice mandates that we develop the best team to deal with these difficult problems. In addition to the teams' skill and preparedness, these cases require courage and a "hate to lose" attitude to have an aggressive approach to achieve a successful outcome.

E-mail (main author): Sim.Franklin@mayo.edu



08:101

Computer-Assisted Tumor Surgery (CATS) in Orthopaedic Oncology: How far have we come?

KC Wong¹

¹⁾ Prince of Wales Hospital, Chinese University of Hong Kong, China (People's Rep Of)

Conventionally, tumor surgeons analyze two-dimensional imaging information and mentally integrate and formulate a three-dimensional surgical plan. It is difficult to translate the surgical plan to the operating room for complex cases with distorted surgical anatomy. Therefore, there is always a strong clinical need for better surgical aids to guide surgeons to achieve exactly what was planned for tumor free margin and bone reconstruction.

CATS has been recently applied in Orthopaedic Oncology and the technology may enable surgeons:

- 1) 3D based planning with multi-modal fused images (anatomical imaging: CT and MR and functional imaging: PET);
- 2) Exact correlation of imaging information to the real anatomical, pathological structures at the surgery under navigation guidance;
- 3) Image-guided bone resection as planned;
- 4) Accurate matching to prosthetic or allograft reconstruction.

Early results suggested that CATS is a safe option to accurately reproduce bone tumor resection as planned. The improved accuracy in executing surgical plans may offer clinical benefits in Orthopaedic Oncology. However, not every resection warrants the use of the technology and CATS may be more useful in technically demanding operations:

- 1) in pelvic or sacral tumors with difficult pathoanatomy
- 2) in hemicortical or joint-preserving tumor resection. More conservative resection is possible with the level of precision that does not compromise oncological principles. This allows patients to retain more native bone and joint for better function.
- 3) in prefabricated custom prosthetic or preparation of allograft reconstructions that are specifically designed to match a bone defect after a preoperatively planned resection.

Comparative studies with long-term follow-up are necessary to confirm its clinical efficacy. Future areas for CATS related studies include

Technology aspects:

- optimizing software system to allow a simple, friendly, all-in-one platform for preoperative 3D planning in orthopaedic oncology;
- the best image modality for image guided navigation surgery;
- the role of patient-specific tumor cutting guides and robotic-assisted system in executing surgical planning.

Clinical impact:

- the evaluation of surgical margin and its related oncological results;
- surgical practice at low-volume tumor centers;
- surgical training in Orthopaedic Oncology.

E-mail (main author): skcwong@ort.cuhk.edu.hk



08:102

Computer Aided Precision Surgery in MSK Oncology

Shekhar Kumta¹, KC Wong¹

¹) The Chinese University of Hong Kong, Hong Kong

The use of Computer aided planning and Navigation assistance during surgery has enabled us to achieve a precision and an accuracy that was hitherto unavailable in the realm of Orthopaedic surgery.

This has translated to an accurate orientation of bony cuts, better seating of prosthetics and perhaps better long term outcomes particularly in the case of prosthetic replacements.

With specific reference to MSK oncology, precision enabled surgery has allowed us to perform an increasing number of joint sparing surgeries, particularly in the pediatric population. This necessarily means an increasing reliance on custom rather than modular prosthesis.

With the integration of advance solid modelling and visualization programs such as MIMICS® we have been able to push the envelope much further than expected. CAOS enables the sync between the surgical plan, the custom-manufactured prosthetic device and facilitates the execution of the grand idea during surgery. Multi-planar resection extreme distal joint –sparing resections and even double-joint sparing solutions have been made possible.

This presentation provides a glimpse of what has been achieved and discusses the essential software and hardware necessary for CAOS. We also discuss the difficulties and the future developments that CAOS surgery may behold for MSK oncologic reconstruction.



08:103

Computer navigation assisted surgery for tumors resection and allograft reconstruction in the extremities

Luis Aponte¹

¹Hospital Italiano de Buenos Aires, Argentina

Introduction: The use of image fusion for computer-assisted bone tumor surgery seems to facilitate not only tumor resection but also bone reconstruction. The purpose of this study is to report our experience in preoperative planning, tumor resection and bone reconstruction with allografts using intraoperative navigation assistance.

Methods: We analyzed sixty-nine patients with bone tumor of the extremities treated using intraoperative navigation assistance. We excluded pelvic tumors in this series. All patients were 3D reconstructed in a virtual platform and planned determining the osteotomy position according to oncology margins in a CT-MRI image fusion. Allografts were selected from our digital bone bank and the allograft osteotomies were also planned preoperatively. Tumor resections and allograft reconstructions were performed using a computer navigation system according to previously planned cuts. Forty-three tumors were localized in the femur, 21 in tibia, 3 in humerus, 1 in cubitus and 1 foot. Reconstructions included 47 intercalary allografts, 18 osteoarticular allografts and 4 APC.

Results: In three patients (4.3%) the navigation was not carried out due to technical problems. In one the crash was secondary to software problem, and in the remaining two cases the crash was secondary to hardware problems. Of the 66 cases where the navigation was performed, the mean registration error was 0.65 mm (range 0.3-1.2). The mean time for navigation procedures including bone resection and allograft reconstruction during surgery was 35 minutes (range 18-65). Histological examinations of all specimens showed a clear tumor margin in all patients.

Conclusion: Our findings suggest that preoperative planning and tumor resection guided by navigation is accurate and useful method for bone tumor resection and reconstruction. Although navigation procedures demands time during surgery, it allows the surgeon to performed accurate cuts in bone tumor resection and allograft reconstruction that reduces the total length of the whole procedure. In our study, the navigation in tumor of the extremities could not be performed in 4.3% of series.

E-mail (main author): luis.aponte@hospitalitaliano.org.ar



08:104

Computer navigation assisted surgery for pelvic and sacral tumours: experience of a tertiary centre

Lee Jeys¹, Gulraj Matharu¹, Rajpal Nandra¹, Rob Grimer¹

¹Royal Orthopaedic Hospital, United Kingdom

Background

Recent reports on the use of computer navigation assisted surgery for the resection of pelvic and sacral tumours have shown promising results, however these conclusions are based on small case series and varied anatomical tumour sites. The study aims were to (1) describe our initial experience with computer navigation assisted tumour surgery, (2) determine the intralesional resection rate when using this technique for primary tumours of the pelvis and sacrum, and (3) determine the early clinical outcomes following tumour resection.

Methods

This prospective study included 23 patients (mean age 53.3 years and 57% male) in which computer navigation assisted surgery was performed for pelvic and sacral bone tumours at a single institution since 2010. Surgery was performed for 18 primary malignant bone tumours (9 chondrosarcoma, 5 sacral chordoma, 3 osteosarcoma, 1 Ewings sarcoma), 3 metastatic tumours, and 2 locally advanced rectal tumours. Preoperative CT and MRI images were fused in the navigation system (Stryker Orthomap 3D Navigation System II) to plan the surgical resection margins. In cases where reconstruction was required custom-made implants (silver coated with a hydroxyapatite collar) were used.

Results

Registration error was less than 1 mm in all cases with no complications related to navigation. Navigation allowed the preservation of sacral nerve roots (n=8), the avoidance of hindquarter amputations (n=3), and resection of otherwise inoperable disease (n=2). Mean total operation time was 260 minutes (range 131-512 minutes). The intralesional resection rate for primary pelvic and sacral tumours was 11% (n=2) with clear bone resection margins achieved in all cases. At a mean follow-up time of 12.4 months (range 1-30 months) three patients (17%) developed local recurrence. Mean time alive from diagnosis was 14.5 months (range 1-38 months).

Conclusions

The present study demonstrated that computer navigation assisted surgery was a safe technique for pelvic and sacral tumours which can reduce the intralesional resection rate (previously 29% at this centre) and provide acceptable short-term rates of local recurrence and complications. It has also allowed more complex resections and reconstructions to be performed. We recommend this technique is worthy of further appraisal in this patient group.

E-mail (main author): lee.jeys@nhs.net



08:105

Computer-assisted planning and patient-specific instruments for bone tumor surgery within the pelvis. Clinical preliminary experience.

Francois Gouin¹, guillaume Odr², Laurent Paul³

¹) Hôtel-Dieu, Centre Hospitalier Universit ²) CHU Nantes, France ³) Visyos, Bruxelles, Belgium

Introduction

Clear margins are one of the major prognosis factors after tumor resection of the pelvis. Clear margins range only from 25 to 88% in the literature, with a high rate of local recurrence.

Computer assisted technology has been recently proposed to surgeons to improve accuracy of bone sections.

Patient specific instrumentation based on pre operative CT and MRI planning has demonstrated its accuracy to replicate preoperatively planned bone cuts on an experimental model.

In this paper, we report our preliminary clinical experience with this technology.

Material and methods

Five patients have been operated for a malignant bone tumor of the pelvis using a patient specific instrumentation based on 3D pre operative tumor delimitation. Bone cuts were chosen by the surgeon and cutting guides positions on bone were chosen by the engineer and surgeon together.

All resection included peri acetabular zone 2, with a posterior trans-sacral cut in 2 cases and a total iliectomy in one case.

Per-operative data and macro and microscopic margins were collected prospectively.

Results

The unique position on bone that corresponds to the patient's specific instrumentation was found very easily with no doubt in 4 cases, with some doubts in one case, and within 5 minutes in all cases.

No per operative complication can be identified as to be in relation with the instrumentation.

The accuracy of the bone cuts, especially the posterior trans sacral cut or the posterior trans iliac cut, allowed a very quick and safe mobilization of the tumor after bone cuts .

In all cases margins were clear of tumor (R0).

No patient recurred.

Discussion

This new technology based on computerized preoperative planning and patient specific instrumentation is promising in terms of per operative technical aid. Our first experience in these challenging localization such as pelvic bone tumor show that we can easily find accurate bone surfaces that support the instrumentation. Moreover the accuracy of bone cuts facilitate tumor mobilization. In all the cases of this short experience, post operative margins were clear in perfect agreement with preoperative planning. A wider experience and longer follow-up is necessary to confirm these findings.

E-mail (main author): fgouin@chu-nantes.fr



O8:106

Computer-assisted planning and patient-specific instruments for bone tumor surgery within the pelvis – an experimental study.

Laurent Paul¹, Pierre-Louis Docquier², Christian Delloye², Xavier Banse², Olivier Cartiaux¹

¹) Université catholique de Louvain ²) Cliniques universitaires Saint-Luc, Belgium

Background

Resecting bone tumors within the pelvis is highly challenging but requires good cutting accuracy to achieve sufficient margins. Computer-assisted technologies such as intraoperative navigation have been developed for pelvic bone tumor resection. Patient-specific instruments, mainly used for arthroplasty, have been transposed to tumor surgery. This experimental study investigated the accuracy of patient-specific instruments for bone cutting during simulated tumor surgeries within the pelvis.

Methods

The experimentations were conducted using synthetic hemipelvic bones (Sawbones). The hemipelvis was CT-scanned to produce a 3D model. A spherical tumor was simulated on the acetabulum. Four cutting planes have been positioned around this tumor including a 10-mm safe margin (Fig.1a). Three bone-specific instruments have been designed (Fig.1b). Their bone-specific surface permitted to fit in unique position on the pelvic model. The flat surface materializes the targeted cutting plane. The instruments were manufactured using rapid prototyping technology. Eight experienced surgeons were asked to perform the tumor resection.

Each performed cut plane was digitized using a coordinate measuring machine (Signum® SL, Mycrona). The accuracy was estimated using the location (maximum distance between the performed and target planes) and the surgical margin (minimum distance between the performed plane and the tumor). The operative time required for the whole tumor resection was recorded.

Results

The location of the performed cut planes with respect to the target planes averaged 1.84 mm [1.31;2.36]. The achieved surgical margins averaged 10.23 mm [9.78;10.67]. The maximum error on achieved surgical margins was 3.12 mm. None of the resections were intralesional. The time required for the resection averaged 6.46 minutes.

Conclusion

This experimental study reports a satisfying accuracy when using patient-specific instruments during cutting of a simulated pelvic bone tumor. The location data demonstrate how patient-specific instruments may help to replicate a preoperative resection planning on a pelvic structure with a good accuracy. The time required for resection shows that this technology is easy to use and does not require a heavy set-up in the operating room. Patient-specific instruments may improve bone tumor surgery within the pelvis and other locations by providing clinically acceptable margins.

E-mail (main author): l.paul@uclouvain.be



08:107

Applications of computer assisted surgery in orthopedic oncology; 130 cases

Paul Jutte¹, Jasper Gerbers²

¹) University Medical Center Groningen ²) MD/PhD Student, UMCG Groningen, Netherlands

The use of computer assisted surgery (CAS) in orthopedics has become more common. Application of CAS in orthopedic oncology, however, is not well described in literature.

In orthopedic oncology CAS can be applied to five types of surgeries. These are excochleations of benign and low-grade malignant tumors, resections of small surface or intra-medulary bone tumors, segmental resections in larger/malignant tumors, reconstructing defects of resections and finally in the placement of tumor prostheses.

Most of the above named types of surgeries require intra-operative imaging. All of them require control over resection margin both for recurrence prevention as to prevent unnecessary bone, and often functionality, loss. Since 2006 we have performed 130 oncological surgeries with CAS.

Most have been excochleations, 64, where CAS replaces fluoroscopy as an intra-operative imaging modality. Some of these patients have been treated with radio frequency ablation before surgery. Advantages over fluoroscopy are real time three dimensional feedback, high-res image and no use of ionizing radiation. It is especially useful in larger lesions or lesions located in the femoral head or pelvis. Currently a study is being performed on patient satisfaction, recurrence and complications.

Another application where CAS has often been used is in resections and segmental resections (36 and 13). These can be preplanned before surgery, incorporating the margin required, and checked intra-operatively. Coloration of the tumor, critical structures is useful to avoid these. Sometimes it's possible with careful planning to spare structures that otherwise probably would not confidently have spared.

With hemicortical resection (6) it's possible to use CAS to exactly copy the shape of the resected bone to an allograft. A Ct scan of one case shows an average gap between host and graft of 0.9 mm (range 0-5.4) along the 6 cm resection.

Finally in 8 cases of imageless use in placement of tumor prostheses it feels greatly helpful in reconstructing the joint line, length and correct rotation.

There were 8 failures with the system or software. Setup time was measured in 47 cases and was on average 6:50 (range 2:26-14:27). In our opinion CAS shows great promise in the field of orthopedic oncology.

E-mail (main author): p.c.jutte@umcg.nl



O8:108

The outcomes of navigation-assisted bone tumour surgery: minimum three-year follow-up

Hae Bong Park¹, Hwan Seong Cho²

¹ Seoul National University Bundang Hospita ² Seoul National University Bundang Hospit, Republic Of Korea

BACKGROUND

Recently there have been several preliminary reports about the application of navigation to the surgery of bone tumours. It is expected that the technique should minimize unnecessary resection, preserve maximum function and achieve good oncological and functional results. However, to date there have been no reports about the longterm outcome of computer-assisted resection of bone tumours. We therefore analysed the oncological and functional outcomes of patients whose malignant bone tumour was excised with the assistance of navigation.

METHODS

We evaluated the oncological and functional outcome of 18 patients, whose malignant bone tumours were excised with the assistance of navigation, and who were followed up for more than three years. There were 11 men and seven women, with a mean age of 31.8 years (10 to 57). There were ten operations on the pelvic ring and eight joint-preserving limb salvage procedures. The resection margins were free of tumour in all specimens. The tumours, which were stage IIB in all patients, included osteosarcoma, high-grade chondrosarcoma, Ewing's sarcoma, malignant fibrous histiocytoma of bone, and adamantinoma.

RESULTS

The overall three-year survival rate of the 18 patients was 88.9% (95% confidence interval (CI) 75.4 to 100). The three-year survival rate of the patients with pelvic malignancy was 80.0% (95% CI 55.3 to 100), and of the patients with metaphyseal malignancy was 100%. The event-free survival was 66.7% (95% CI 44.9 to 88.5). Local recurrence occurred in two patients, both of whom had a pelvic malignancy. The mean Musculoskeletal Tumor Society functional score was 26.9 points at a mean follow-up of 48.2 months (22 to 79).

CONCLUSIONS

We suggest that navigation can be helpful during surgery for musculoskeletal tumours; it can maximise the accuracy of resection and minimise the unnecessary sacrifice of normal tissue by providing precise intra-operative three-dimensional radiological information.

E-mail (main author): mdchs111@snu.ac.kr



09:101

Sports activity levels of healthy long term survivors with modular tumor endoprostheses following osteosarcoma of the knee joint

Nikolaus Lang Lang¹, Gerhard Hobusch¹, Reinhard Schuh¹, Martin Dominkus¹, Reinhard Windhager¹, Jochen Hofstaetter¹

¹Medical University of Vienna, Austria

BACKGROUND:

Little is known about participation in sports following limb-salvage surgery for osteosarcoma of the knee joint. The purpose of this study was to evaluate sports activity in long-term survivors with modular tumor endoprosthesis of the knee joint following osteosarcoma.

METHODS:

This retrospective single-center study includes 27 patients (13 m, 14 f) with osteosarcoma of the knee joint who were treated between 1995 and 2005 with an implantation of a modular tumor endoprosthesis. The average age at the time of surgery was $25,5 \pm 13,5$ (12,6 - 60,1) years and mean follow up period was $11,2 \pm 3,7$ (5,3 - 15,6) years. The tumor was located at the distal femur in 16 cases and at the proximal tibia in 11 cases. We assessed type frequency and duration of sports prior to osteosarcoma, 1, 3 and 5 years post surgery. Moreover the assessment included sports activity scores. Furthermore, the effect of complications on activity levels was assessed.

RESULTS:

Prior to osteosarcoma 89% (24/27) of the patients were regularly performing sports. At 1-, 3- and 5-years following osteosarcoma, 33%, 74% and 89% respectively were able to perform sports. There was a change from high to low impact sports. The most common types of sports postoperatively were bicycling and swimming. At five years post surgery patients reached their maximum post op levels of UCLA Activity Score (UCLA), Tegner Activity Score (TAS) and modified Weighted Activity Score (WAS). We found significant correlations between pre- and postoperative sports activity levels (UCLA: $r = 0,62$ ($p < 0,0005$); TAS $r = 0,69$ ($p < 0,0001$); WAS $r = 0,49$ ($p < 0,01$)). Fourteen patients (51%) had to undergo revision surgery. However neither oncological nor non-oncological complications had a significant effect on sports activity levels. Moreover no sports activity related complications were found.

CONCLUSION:

Long-term survivors of osteosarcoma of the knee joint who underwent limb-salvage surgery with a modular tumor endoprosthesis can achieve high levels of sports activity. However, the type of sports, duration change and recovery takes up to five years. Patients who were very active prior osteosarcoma tended to be more active postoperatively.

E-mail (main author): nikolaus_lang@hotmail.com



09:102

Sports activity levels in long-term survivors of Ewing sarcoma in spine, pelvis and lower extremity

Gerhard Hobusch¹, Nikolaus Lang², Kerstin Gruber², Martin Dominkus², Reinhard Windhager², Jochen Hofstaetter²

¹ Medical University of Vienna ² MUW, Austria

Background:

Quality of Life and functional outcome became a field of interest in patients with Ewing sarcoma (EWS). Sports is an important part in the lives of young adults. However, currently there are no data available with regard to sports activity levels of patients with EWS.

Methods:

Sports activity levels in patients with EWS after multimodal treatment including surgical resection and radio-chemotherapy treated at a single institution with a minimum follow-up of five years were retrospectively assessed. 35 survivors (14 f/ 21 m) with an average age of 18 years and a mean follow-up time of 15,8 years following EWS were included. The tumors were located in spine (n=5), pelvis and proximal femur (n=18), knee joint and lower leg (n=12). The surgical procedures included surgical resections alone (n=16) or surgical resection with biological reconstruction (n=5) or endoprosthetic reconstruction (n=14).

Results:

One year before surgery and five years post surgery 34 out of 35 Patients (97,1%) were performing athletic activity. The most common types of sports were cycling, swimming and hiking. Depending on the location and the type of surgical procedure two different patterns of postoperative sports activity levels were found. Patients with resections in spine, pelvis and femur and biological and endoprosthetic reconstructions in the proximal femur and knee improved in UCLA Activity score from 3,9 to 6,3 points (1 year postoperative latest follow up) in Tegner activity score from 2,6-4,3 points and in modified Weighted Activity Score from 2,3-5,3 points in the course of sports activity assessments 1, 3 and 5 years postoperative. Patients who were the most active preoperatively tended to do more sports post-operatively (p=0,42). Patients with megaendoprosthetic reconstruction of the pelvis, fibula for tibia reconstructions and after resection of the fibula, sports activity remained at a low level post-operatively.

Conclusion:

Healthy long-term survivors can achieve high levels of sports activity following EWS. The localization of the tumor significantly determined the sports activity levels achieved. Preoperative sports activity levels significantly correlated with postoperative sports activity levels. This information will help surgeons as well as newly diagnosed patients when it comes to long-term expectations following EWS.

E-mail (main author): gerhard.hobusch@meduniwien.ac.at



09:103

Patient Outcome Following Inpatient Rehabilitation within the London Sarcoma Service

Abigail McCarthy¹

¹) Royal National Orthopaedic Hospital, United Kingdom

Research suggests physical activity during or after cancer treatment improves physical and psychological wellbeing, reduces risks of consequence of treatment and improves survival rates, hence Macmillan launched the Move More campaign in 2011. The National Cancer Survivorship Initiative also identified a requirement for change to the care pathway of patients to offer a more holistic approach. The National Cancer Action Team have also published rehabilitation guidelines for sarcoma patients (2012).

Observing patients returning to clinic following completion of adjuvant treatment it was noted full functional potential was often not achieved. Reductions in funding of local outpatient services meant patients were often dismissed due to non-attendance or were discharged after 6 sessions. The London Sarcoma Service recognised the requirement to broaden the rehabilitation services provided to oncological orthopaedic patients and developed a focussed one week in-patient rehabilitation programme with OP follow up.

The therapy led programme includes joint initial assessment with PT and OT to address therapeutic, functional and quality of life issues. Core stability, gait re-education and cardiovascular endurance are common focus areas to achieve goals as diverse as equestrian pursuits, bathing, driving and return to work. The presence of the ASPIRE training centre on site is helpful in allowing patients to gain confidence in use of leisure facilities when returning to their local community.

The results from 10 patients who have utilised this programme will be presented including a thematic analysis of patient concerns and goals following assessment. Patient satisfaction has been high and use of the patient specific functional scale outcome measure has demonstrated a significant improvement in patient function during the week. Patients have been followed up to ensure that their progress has been maintained and continued.

E-mail (main author): Abigail.McCarthy@rnoh.nhs.uk



09:104

Functional outcome and quality of life after resection of the proximal humerus in musculoskeletal tumours

Imre Antal¹, Krisztián Szalay¹, János Kiss¹, Tamás Perlaky¹, Miklós Szendroi¹

¹ Semmelweis University, Hungary

BACKGROUND

There are several successful methods for reconstruction of the proximal humerus after tumor resections, but the function of the shoulder joint can only be restored partially. The functional outcome after proximal humeral resection depends on the type of reconstruction, but also on the resection of the rotator cuff and the deltoid muscle.

METHODS

We reviewed 84 patients who underwent proximal humerus resection in the Department of Orthopaedics at Semmelweis University (Budapest, Hungary) from 1981 to 2012. Medical records were reviewed. Functional evaluation was done according to the Musculoskeletal Tumour Society (MSTS) system, health status was assessed by the Short Form-36 questionnaire.

RESULTS

Hemiarthroplasty with tumour endoprosthesis was carried out in 43 cases, autologous fibular transposition was done in 25, reverse prostheses-allograft composite in 6 and osteoarticular allograft in 10 cases. These were done to treat primary tumours in 56 cases and metastases in 28 cases. The mean age was 32 years (range 10-73 years) in patients with a primary tumour and 65,4 years (range 30-76 years) in those with metastases. Mean follow-up was 96 months (range 6-254 months). The mean MSTS score was 84% for reverse prostheses-allograft composite, 67% for tumour endoprosthesis, 64% for osteoarticular allograft, and 70% for autologous fibular transposition. Major complications occurred in 40% of the osteoarticular allograft group, in 11% of the tumour endoprosthesis group and in 24% of the autologous fibula group. There were no complications in the group reconstructed with reverse prostheses-allograft composite.

CONCLUSION

According to both the literature data and our own results, it seems that after proximal humeral resections the best results can be achieved by reverse prostheses-allograft composite or fibular transposition, when the function of the rotator cuff was preserved and the fibula did not resolve. After humeral resection with the implantation of a tumour endoprosthesis or osteoarticular allograft the function of the shoulder remained moderate because the rotator cuff was damaged. The overall satisfaction was generally good after all types of proximal humeral reconstruction. Patients can compensate extremely well by using the preserved joints and the contralateral upper limb; therefore, patient satisfaction does not rely on shoulder function alone.

E-mail (main author): krisztian.szalay@gmail.com



09:105

Functional results of Modular Prosthesis Replacement for Malignant Tumors of the Extremities

Oleg Vyrva¹, Roman Malik¹, Victor Burlaka¹, Igor Shevchenko¹

¹) Sytenko Institute, Ukraine

Background:

The objective of this study was to determine the long-term function and complications associated with segmental resections performed for malignant bone tumors reconstructed with Modular Prostheses.

Methods and Materials:

We retrospectively reviewed the records of 166 patients with Modular Prosthesis Replacement from 2002 to 2012. There were 92 males and 74 females. Mean age at the time of diagnosis was 39 years (range 7-75 years). Diagnoses included 64 osteosarcomas, 58 metastatic lesions, 38 chondrosarcomas, 4 Ewing's sarcomas, 2 synovial sarcomas. 166 primary and 24 revision Modular Prostheses were placed with 56 in the distal femur, 32 in the proximal femur, 30 in the proximal tibia, 19 in the proximal humerus, 9 in the distal radius, 5 in the femur diaphysis, 5 in the distal tibia, 5 in the distal humerus, 2 in the diaphysis humerus, 2 in the proximal ulna, 1 in the proximal radius. Mean follow-up was 5,4 years (range 1-10 years). Treatment was individualized depending on patient presentation. The MSTS and TESS scores were used to calculate functional results.

Results:

13 patients (7,8%) had died at last follow-up. 21 patients (12,7%) had had local tumor relapses. 20 patients (10,5%) had had prostheses failures and 21 patients (11,1%) had had infection complications. 11 patients (6,6%) had had amputations. The mean MSTS score for the upper extremity were (67 ± 9) %, for low extremity (76 ± 16) %. The mean TESS score for the upper extremity were (70 ± 11) %, for low extremity (79 ± 15) %.

Conclusion:

The Modular Prosthesis Replacement for malignant bone tumors has a high rate of good functional results at long-term follow-up. Patients who underwent revision surgery had worse function than patients who retained their initial Modular Prosthesis Replacement.

E-mail (main author): vyrva@online.kharkiv.com



09:106

Early rehabilitation using temporal external fixation following resection of pelvic sarcoma

Toshiyuki Kunisada¹, Yoshimi Katayama², Ken Takeda³, Joe Hasei³, Masuo Senda², Toshifumi Ozaki³

¹ Okayama University Graduates Schools ² Rehabilitation, Okayama University ³ Orthopaedics, Okayama University, Japan

INTRODUCTION:

Pelvic resection for sarcoma sometimes requires prolonged bed rest or immobilization postoperatively to stabilize the bone and/or soft tissue reconstruction. Massive implantation to stabilize the pelvic reconstruction may result in high risk of deep infection. We applied temporal external fixation (EF) for patients who underwent pelvic resection including P1 and/or P2 region to get early postoperative function.

PATIENTS:

8 cases with pelvic sarcoma were temporally applied with EF following tumor resection and reconstructive surgery, since 2008. There were 5 patients with P123 resection, 1 with P12 resection, 1 with P23 resection, and 1 with P1 resection. The pins were inserted into affected femur and healthy contralateral ilium. Pathologic diagnosis consisted of 3 chondrosarcoma, 2 osteosarcoma, 2 Ewing sarcoma, and 1 undifferentiated sarcoma. 7 patients underwent resection arthroplasty (hip transposition), and 1, fibula graft for P1 resection. EF was removed and weight-bearing started 6-8 weeks postoperatively. We assessed postoperative achievement of activities of daily living and MSTs score.

RESULTS:

Average limb length discrepancy was 5.5cm. Average postoperative follow-up was 23 months. Sitting on bed was possible averagely on Day 7, standing along bed on Day 8, transfer to wheel chair on Day 12, Walking exercise using parallel bars on Day 22, and walking using crutches on Day 53. At removal of EF, image intensifier assessment showed that all reconstructive procedures were stable enough to start weight-bearing. At final follow-up, 4 patients can walk without any supports, 3 with one crutch, and 1 with two crutches. There was no major complication related to EF. Average MSTs score was 69%.

DISCUSSION:

Hip transposition originally required about 4 week immobilization in bed with cast or brace to stabilize the reconstruction. Fibular graft for P1 resection also reportedly needed prolonged immobilization if there was less stable implantation. Temporal EF could stabilize bone and soft tissue reconstruction after pelvic resection, resulting in less pain for patients. Pelvic reconstruction with temporal EF can lead to early physiotherapy, and may result in better rehabilitation without major complication.

E-mail (main author): toshikunisada@gmail.com



O9:107

Can Immunohistochemical characterisation of liposarcoma guide the selection for novel therapy based on the P53 – MDM interactions?

Nader Touqan¹, Rajgopal Achuthan², William Merchant², Kieran Horgan², Ian Carr¹, Rashda Anwar¹, Alexander F Markham¹

¹ University of Leeds ² Leeds Teaching Hospitals, United Kingdom

Background

Inactivation of wild type P53 by its main cellular inhibitors (MDM2 and MDMX) is a well recognised feature of tumour formation in liposarcomas. MDM2 over-expression has been detected in approximately 80% of liposarcomas but only limited information is available about MDMX over-expression. To date, we are not aware of any study that has described the patterns of MDM2 and MDMX co-expression in liposarcomas. Such information has become more pertinent as various novel MDM2 and / or MDMX single and dual affinity antagonist compounds are emerging as an attractive means of potential targeted therapeutic strategies.

Methods

After obtaining the appropriate ethical approvals and with informed consents, we analysed a series of 61 cases of fully characterised liposarcomas of various subtypes by immunohistochemistry to assess the simultaneous expression levels of P53, MDM2 and MDMX.

Results

50 cases over-expressed MDM2 and 42 of these co-expressed MDMX at varying ratios. The relative expression levels of the two proteins with respect to one another were subtype-dependent. This directly affected the detected levels of P53 in two distinct patterns. Diminished levels of P53 were observed when MDM2 was significantly higher in relation to MDMX, suggesting a dominant role for MDM2 in the degradation of P53. Higher levels of P53 were noted with increasing MDMX levels suggesting an interaction between MDM2 and MDMX that results in a reduced MDM2 efficacy in degrading P53. Despite the different genetic alterations involved in the cancerous transformation of the different subtypes of liposarcoma, it is striking that the above patterns applied to all subtypes with a statistically significant negative correlation between MDM2:MDMX ratio and P53 expression ($p < 0.001$).

Conclusion

The results suggest that dynamic complex interactions between MDM2 and MDMX proteins may directly affect the cellular expression levels of P53. This therefore invites careful characterisation of these markers in tumours when considering in-vivo experimental evaluation of novel blocker compounds for MDM proteins as a therapeutic strategy to restore wild type P53 functions.

E-mail (main author): n.touqan@leeds.ac.uk



09:108

Inhibition of sirtuin-1 activity as a potential therapeutic strategy for pediatric soft tissue sarcomas.

Bertha Brodin¹, Limin Ma¹, Barry Wolahan¹, Wessen Maruwge¹, Sonia Lain¹

¹) Karolinska Institutet, Sweden

Sirtuins are a NAD⁺ dependent class III histone deacetylases with a variety of histone and non histone substrates.

Seven sirtuins (sirT 1-7) have been identified in mammals. SirT1 has been implicated in the regulation of glucose and lipid metabolism during cellular stress conditions like fasting and calory restriction. In addition of its functions in cell metabolism, SirT 1 has been implicated in tumor progression since it mediates the deacetylation of several cancer associated transcription factors like p53, NFkB and FOXO proteins.

We have analyzed the expression of sirT1 and sirT2 in a serie of synovial sarcoma tumors and cell lines and evaluated the activity of the sirtuin inhibitor tenovin-6, in synovial sarcomas and rhabdomyosarcomas. We found that sirT1 was overexpressed in synovial sarcomas biopsies and cell lines in comparison to normal mesenchymal cells. Exposure of synovial sarcoma and rhabdomyosarcoma cell lines to tenovin-6, inhibited tumor cell proliferation and induced the expression of the cyclin dependent kinase inhibitor p21 independently of p53 expression and acetylation. Tenovin 6 anti-tumour activity was associated with decreased de-acetylating activity of nuclear and cytoplasmic sirtuins including sirT1.

Combination of tenovin 6 with doxorubicin had a synergistic anti-proliferative effect in synovial sarcomas. In addition, the combination of tenovin-6 with the multikinase inhibitor Sorafenib, had a significant anti-tumor growth effect on synovial sarcoma and rhabdomyosarcoma cell lines. Rhabdomyosarcoma xenografts treated with tenovin 6 had a decreased tumour mass as compared to placebo treated controls. The treated tumors up-regulated cytoplasmic sirT2 and displayed nuclear tranlocation of p53.

Our results indicate that overexpression sirT1 can be associated with the pathogenesis of synovial sarcoma and rhabdomyosarcoma and that the pharmacological inhibition of sirtuin activity is a potential therapeutic strategy for these tumors.

E-mail (main author): bertha.brodin@ki.se



09:109

Genomic instability and characteristic DNA methylation pattern in chordoma

Beate Rinner¹, Andreas Weinhaeusel², Birgit Lohberger¹, Pulverer Walter³, Fischer Carina¹, Scheipl Susanne¹, Meditz Katharina¹, Liegl Bernadette¹, Leithner Andreas¹

¹ Medical University of Graz ² AIT-Austrian Institute fo Technology ³ AIT Austrian Institute of Technology, Austria

Chordomas are rare mesenchymal tumors occurring exclusively in the midline from clivus to sacrum. Early tumor detection is extremely important as these tumors are resistant to chemotherapy and irradiation. Despite continuous research efforts surgical excision remains the main treatment option. Because of the often challenging anatomic location early detection is important to enable complete tumor resection and to reduce the high incidence of local recurrences. The aim of this study was to explore whether DNA methylation, a well-known epigenetic marker, may play a role in chordoma development and if hypermethylation of specific CpG islands may serve as potential biomarkers correlated with SNP analyses in chordoma. The study was performed on tumor samples from ten chordoma patients. We found significant genomic instability, it was interesting to see that all chordomas showed a loss of 3q26.32 (PIK 3CA) and 3q27.3 (BCL6) thus underlining the potential importance of the PI3K pathway in chordoma development. By using the AITCpG360 methylation assay we elucidated 20 genes which were hyper/hypomethylated compared to normal blood. The most promising candidates were nine hyper/hypomethylated genes C3, XIST, TACSTD2, FMR1, HIC1, RARB, DLEC1, KL, and RASSF1. In summary, we have shown that chordomas are characterized by a significant genomic instability and furthermore we demonstrated a characteristic DNA methylation pattern. These findings add new insights into chordoma development, diagnosis and potential new treatment options.

E-mail (main author): beate.rinner@medunigraz.at



09:110

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

Marusya Lieveld¹, Liesbeth Ceelen¹, Maria-Serena Benassi², Piero Picci², Gwen Sys³, Pancras Hogendoorn⁴, Ramses Forsyth¹

¹) Pathlicon, Belgium ²) IOR ³) University Ghent, Italy ⁴) LUMC, Netherlands

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.

E-mail (main author): r@forsyth.be



O10:101

Osseointegration: An overview

Rickard Brånemark¹

¹, Sweden

Osseointegration has been in successful clinical practice for dental applications since 1965. The method of osseointegration is also successfully used for permanently skin-penetrating applications in the head and neck area including treatment with bone-anchored hearing aids and for anchorage of prosthetic ears and eyes.

Treatment with osseointegrated amputation prostheses has been performed in Sweden since 1990. More recently centers in the United Kingdom, Australia, Spain, Hungary, France, Chile, Denmark, Belgium and Holland have started to use the treatment. In 1999, a prospective clinical investigation was started at the Sahlgrenska University Hospital in Gothenburg, Sweden on patients treated with transfemoral OI-prostheses. The patients are treated in two surgical sessions followed by rehabilitation with a total treatment period of approximately 12 months. At the first surgery a titanium implant (fixture) is inserted in the residual bone and left unloaded for about six months. At the second surgery a titanium rod (abutment) is inserted into the distal end of the fixture and is then penetrating the skin. The external prosthesis is connected to the abutment with an attachment device. After surgeries the patient undergoes a period of rehabilitation during six months with gradually increased weight bearing and prosthetic activities.

The risks with the treatment are loosening, deep infection, superficial infections, skeletal fracture and mechanical failures. The benefits are in many instances related to the removal of the socket as attachment of the prosthesis to the stump. The amputee no longer has skin sores, pain when loading, and problems with stump volume changes. Further, normal sitting comfort and normal hip range of motion is regained. All these changes lead to a significantly improved quality of life for the individual with transfemoral amputation.

E-mail (main author): rickard.branemark@orthop.gu.se



O10:102

A decade's experience with the Integral Leg Prosthesis (ILP): a case series study of design modifications to prevent infection

Horst Aschoff¹, Dora-Lis Juhnke², James Beck³

¹⁾ Sana Clinics Lübeck, Germany ²⁾ Norwest Advanced Orthopaedics, Norwest P, Australia ³⁾ Department of Orthopaedics, University o, United States

Methods

Between 1999 and 2011, 54 patients with above-knee (AK) amputations were fitted with ILPs by a single surgeon. Throughout a twelve year case series different changes to improve implant design and surgical technique has been empirically driven and clinically based to reduce the technique's inherent risk of an ascending infection. We divided patient's receiving different designs and procedures in Group I and Group II to statistically compare planned and unplanned surgical interventions.

Results

The data demonstrates an initially high rate of stoma-associated infections. However, the changes made to the design as well as the surgical technique could effectively reduce this risk; between January 2009 and December 2011 no operative intervention for stomal soft tissue or deep bone infections became necessary.

Discussion

Bone-anchored prostheses have to meet the challenge of successful osseointegration as well as the risk of a stoma-associated infection. Using the ILP, formerly known as the Endo-Exo-Femurprosthesis, a stable integration into the remaining femur has been accomplished. The risk of an ascending infection could be dramatically decreased altering the implant's surface at the soft tissue-prosthesis interface and adjusting the surgical approach accordingly. We consider the ILP a safe alternative to the socket

E-mail (main author): horst.aschoff@sana.de



O10:103

Case presentations of the Integral Leg Prosthesis (ILP): achievements and pitfalls

Horst Aschoff¹, Dora-Lisa Juhnke², Munjed Al Muderis²

¹) Sana Clinics Lübeck, Germany ²) Norwest Advanced Orthopaedics, Norwest P, Australia

Methods

This osseointegrated technique involves two surgical steps and a following rehabilitation process where the patient has to learn how to mobilize and walk again freely with the bone-guided implant. In between 01/1999 and 01/2013 altogether 95 patients were treated with the ILP by two surgeons located in Lübeck, Germany and Sydney, Australia. We present special cases.

Results

To this point we performed the ILP procedure on 88 trans-femoral and 7 trans-tibial amputees. Special challenges include implant failure, fractures, particular bone conditions and amputation levels, missing osseointegration and bilateral supplies. These challenges impose the need to constantly re-evaluate patient's situations and build up a close relationship with them to have positive and satisfying results that meet reasonable expectations.

Discussion

Amputation and following rehabilitation always has a deep and life-changing impact on the affected individual and each situation has to be understood and dealt with as being a unique story, which involves unique people. Given the more than 100 patients provided with the ILP worldwide it by now seems admissible to describe some procedures as rather standard while others stand out in regards to different aspects of patient's physical, psychological, social or work-related conditions. Their clinical and follow-up stories that are linked to experiencing an ILP are inevitable to be told to think about and learn from them.

E-mail (main author): horst.aschoff@sana.de



O10:104

Bone Anchored Prosthesis with the Osseointegration Technique in Transfemoral Amputees. Results from the Prospective OPRA Study

Örjan Berlin¹, Peter Bergh², Björn Gunterberg², Kerstin Hagberg², Björn Rydevik², Rickard Brånemark²

¹) Sahlgrenska University Hospital ²) Sahlgrenska Univ Hospital, GOT, SWE, Sweden

Background. Transfemoral amputations due to trauma or tumor surgery often cause problems with conventional socket prostheses. In 1999 we initiated the prospective OPRA study (Osseointegrated Prosthesis for Rehabilitation of Amputees) using standardized surgery, equipment and rehabilitation program.

Methods. The surgery consists of a two-stage procedure. First a titanium screw (fixture) is inserted into the remaining skeleton (S1 operation). Six months later a second implant (abutment) is inserted into the first, allowing it to penetrate the skin (S2 operation). Gradual increase of loading are done over a 6-month period.

Results. The OPRA study includes 51 patients with 55 implants (1999–2010). Follow up is 2 years. Four implants have been removed due to loosening (3) or infection (1). One patient was lost to follow-up, two were excluded. The implant survival was 92 % (48/52). The patients had an average of one superficial infection every two years, successfully treated conservatively in all cases. There were 6 deep infections in 4 patients. All but one were successfully treated by conservative means. Four patients had 9 mechanical complications (bent or fractured implant parts) and 3 skeletal fractures occurred. Prosthetic use, prosthetic functions and global quality of life were all significantly improved ($p < 0.001$) and prosthetic problems were reduced ($p < 0.001$).

Conclusion. The implementation of a standardized osseointegrated surgical technique and the graded rehabilitation protocol is of importance for the promising results. The benefits are related to the removal of the socket as attachment of the prosthesis to the stump. The amputee no longer has skin ulcers, pain when loading, and problems with stump volume changes. Normal sitting comfort and normal hip range of motion can be expected. All these changes lead to a significantly improved quality of life for the individual with a transfemoral amputation.

E-mail (main author): orjan.berlin@gmail.com



O10:105

Osseointegration is a viable solution for rehabilitating patients post tumor-related amputations

Munjed Al Muderis¹, Dora-Lisa Juhnke², Horst Aschoff³, Ludger Gerdesmyer⁴

¹) Macquarie University, Australia ²) Charite ³) Lubeck ⁴) Keil, Germany

BACKGROUND

Transcutaneous osseointegration is an innovative technology that has been successfully used for amputees since the 1990s to overcome the problems associated with the conventional socket prosthesis. Between 1999 and 2011 we performed one hundred operations using this technology, 10% of these patients were amputated due to musculoskeletal tumors.

METHODS

Between 1999 and 2011 we performed one hundred osseointegration procedures in 94 patients. These surgeries were performed in two centers: Lübeck, Germany and Sydney, Australia by the two principle surgeons acquainted with this technology. It involves the insertion of a transcutaneous intramedullary implant into the remaining bone; the implant's most distal external aspect then serves as a hard point for further prosthetic attachment rather than the entire soft tissue mantle of the remaining limb.

Altogether there were 74 males and 20 females. The age range was between 17 to 76 at time of implantation. Ten of our patients had amputations due to tumors with an age range from 32 to 73 at time of implantation. Preoperative assessments included medical, psychological and radiological examinations. All patients underwent the standardized two-stage procedure with a six-week interval. All patients were allowed early mobilization and full weight bearing two weeks after the second stage surgery.

RESULTS

Overall, there was a high level of patient satisfaction. All patients except one returned to pre-amputation activities. All patients except one have retained the implant up to date. In the remaining patients gait improved. No infections to date occurred in the patients that underwent surgery after 2009 since a new implant design was used. All patients regained osseoperception and reduced phantom pain. Skin irritations due to the old socket prosthesis have completely recovered in all patients.

CONCLUSION

Osseointegrated prostheses are an excellent alternative and potentially will be the first choice for many amputees in the near future. We have demonstrated that this technology enables patients to regain much of their freedom in mobility without compromising the mechanical stability of osseointegration. The technique constitutes a versatile option for people suffering limb loss secondary to malignancy due to the relative young age of these patients at time of amputation.

E-mail (main author): munjed@me.com



O10:106

Rehabilitation in patients with conventional amputation versus patients with osseointegrated prostheses

Kerstin Hagberg¹

¹ Sahlgrenska University Hospital, Sweden

Individuals with transfemoral amputation are conventionally supplied with a prosthesis that is suspended to the residual limb via a socket. Today prosthetic attachment can also be directly to the residual skeleton by using the method of osseointegration and in this case no prosthetic socket is needed. This presentation will describe the main differences between the two methods when it comes to the prosthetic rehabilitation in individuals with transfemoral amputation.

E-mail (main author): kerstin.hagberg@vgregion.se

O10:107

Osseointegration: The experience of the first seven patients in Leiden

Nicolette Leijerzapf¹, Hans Arendzen¹, Dies Boonman¹, Eric Vermeulen¹, Sander Dijkstra¹

¹ Dept. of Orthopedic Surgery, Leiden University Medical Center, Leiden, the Netherlands

Introduction: Bone anchored prosthesis based on osseointegration is an innovative treatment for amputees with socket problems due to their prosthesis. Osseointegration for amputees has been performed in Sweden since 1990. The OPRA procedure, the Osseointegrated Prosthesis for the Rehabilitation of Amputees, includes two surgical stages followed by rehabilitation. The first stage (S1) is to place a titanium implant (the fixture) into the cavity of the bone. S2, the second stage, performed 6 months later; the abutment screw is inserted into the distal end of the fixture and protrudes through the skin. Also remodelling of the soft tissue must be performed. The goal of this procedure is to click the prosthetic limb directly onto the abutment screw without wearing a prosthetic socket. The rehabilitation schedule, during 6 months, is managed by the OPRA protocol and physical therapists. The rehabilitation physician and orthopaedic surgeon include the patient for the osseointegration. Contra indications are: arterial problems, diabetes, infections, obese, smoking, use of corticosteroids, recent malignant tumor, immunosuppressive therapy, renal failure and poor bone quality. Mental stability is very important.

Methods: In Leiden we started in September 2011. We treated 7 patients, 6 transfemoral and 1 transtibial amputees. The median age was 49 (31-67). Two patients had amputations due to a tumor and 5 due to trauma. The median follow up was 9,5 (2-17) months.

Results: Three patients had temporary wound problems. Two patients walk with prosthesis without any problem. They have hardly complaints, no pain, no skin problems, better walking pattern, easy click-fixation of the prosthesis and a new phenomenon: osseoperception. This leads to a better quality of life. Three are at the end of their rehabilitation period and start their mobilisation with crutches. Two patients just started with the rehabilitation.

Conclusions: The two patients, who had finished the rehabilitation period, had a spectacular outcome. A good collaboration between orthopaedic surgeon, rehabilitation physician, physical therapists, nurse practitioner and prosthetist is mandatory for the success of osseointegration.



O11:101

The use of Additive Layer Manufacturing (ALM) for the fabrication of specialized limb salvage implants

Paul Unwin¹, Sudha Shunmugam², Kirti Wagjian², Abtin Eshraghi²

¹ Stanmore Implants ², United Kingdom

Additive Layer Manufacturing (ALM) is becoming an important fabrication technique for orthopaedic implants and is particularly suited to specialised implants such as those used in limb salvage. ALM has already proven its capability for producing small complex components for the aerospace industry. The ALM process uses a high-powered laser or electron beam to selectively sinter fine powder such as titanium alloy in ultra-thin layers enabling complex free-form components to be built layer by layer. ALM is ideal for one off components such as ingrowth lattices that would be impossible using conventional subtractive manufacturing techniques.

This aim of this study was to describe the adoption of ALM into the design and fabrication process of titanium alloy limb salvage devices.

Prior to the clinical use of ALM, extensive metallurgical and mechanical testing was undertaken.

The first clinical application of an ALM titanium alloy implant was undertaken in November 2010. A 62 year old male with a chondrosarcoma of periacetabulum required an extensive resection of the ilium and sacro-iliac joint saving only a small part of the superior pubic ramus. A 3-dimensional model was created from CT scans from which the implant was designed. Key design features included extensive lattice structures at the SI joint and pubic ramus bone interfaces, transverse sacral bolts and a large medialised acetabular socket. The lattices were hydroxyapatite coated and the device was implanted with the aid of navigation. Following an uneventful rehabilitation, at 6 months the patient was full weight bearing with a stick. At 24 months the patient remains active and radiographically there is the appearance of bony ingrowth into the lattice structure.

To date, 7 scapula and 11 pelvic replacements have been implanted. The early use of this advanced manufacturing route for patient specific limb salvage implants has been very encouraging as it enables the engineer to produce a more anatomical conforming implant with integral 3D lattice structures for bone and soft tissue integration. It is anticipated that laser-based ALM will be a key process in the development of the next generation of limb salvage implants.

E-mail (main author): paul.unwin@stanmoreimplants.com



O11:102

Basic Sciences and Bioengineering of Microwave Hyperthermia in Limb Salvage

Edmund Y.S. Chao¹

¹ Mayo Clinic & Johns Hopkins University, United States

The use of low and deep-set heat generated by high frequency alternating current as a means to destroy cancer cells was first proposed by Nikola Tesla in 1891 termed as "Medical Diathermy". This innovative idea has gone through a long evolution in medical oncology now defined as "Hyperthermia" using different method to generate and deliver the heat to treat both resectable and un-resectable tumor. For musculoskeletal tumor, the most desirable method is the microwave dielectric heating method using pointed antenna to penetrate and reach various parts of the afflicted connective tissues. Although the scientific basis for tumor cell ablation and the technical aspects in limb salvage application are insufficiently established, QY Fan, of Xi'an, China has pioneered this method in extensive clinical trial since the early 1990s with impressive results. To assure a safe ablation margin in comparison to regular en bloc resection method, over-heating was implemented in all cases. Theoretically, hyperthermia has several major potential advantages: 1) optimal heat delivery could achieve safe and effective tumor ablation; 2) low temp treated bone, though completely devitalized, maintains greater biomechanical strength and with higher potential to regenerate; 3) the remaining osseous structure after curettage serves as biologic scaffold making reconstruction easier and with less metallic implant; 4) retain muscle-to-bone attachment to allow easier regeneration for better functional results.

However, there are several concerns that must be adequately addressed before widespread clinical trials could be safely recommended. These are: 1) assurance of tumor ablation to prevent local recurrence; 2) improvement in antenna design and surgical application; 3) ability to achieve optimal heat dispersion throughout the tumor bed with sufficient and desirable safety margin; and 4) adequate protection of normal tissue and organ surrounding and adjacent to the treatment field. These concerns could all be satisfactorily resolved through basic sciences research and bioengineering development. Using proper animal models and tissue type, different heat conduction and dispersion properties under realistic physiological conditions can be quantified and validated. Through advanced imaging techniques and simulation technology, pre-treatment planning and intraoperative execution steps can be worked out for optimal tumor cell ablation in different anatomical location and extend. Various cooling methods are available to protect the connective tissues and structure such as the cartilage, ligaments, tendon-to-bone junction etc. For the vessels, nerves, and spinal cord closely imbedded within the cancerous tissue bed may be managed by the irreversible electroporation technique currently explored by QY Fan.

Hyperthermia is a promising method to bring the current standard and success of limb salvage to a new level. To reach there, coordinated R&D effort is mandatory as no single institution can meet all the prerequisites in basic science, engineering technology and clinical trial to make this method well accepted. Musculoskeletal tumor is a relatively small field to attract major funding from available sources. Multi-institutional collaboration with foundation and industrial support may offer the opportunity to bring this practical, most important but low payback venture to reality. Thus far, it has been a dedicated effort of a single person and institution. However, their outcome we all have witnessed deserves proper consideration and support. Although the current science and technology of applying this method are limited, more clinical trials using the present method and instruments on difficult malignant cases involving the pelvis and the aggressive benign GCT in the long bones should be encouraged to solidify the theoretical advantages for the purpose of enhancing the confidence amongst the orthopaedic oncologists. This is one of the most desirable fields to harness the available high-tech in bioengineering, thus making computer-aided and robotic assisted limb salvage surgery a practical reality!



O11:103

Microwave Hyperthermia Applied to Limb-salvage Surgery for Malignant Bone Tumors

Qing-Yu Fan¹, Boan Ma¹, Yong Zhou¹, Minhua Zhang¹, Tong Tao Yang¹, Hua Long¹, Lian He Zheng¹, Zhao Li¹

¹ Tangdu Hospital, China

Background: Limb-salvage surgery has been widely used for the last several decades, and proved to be an effective way to treat malignant bone tumors. However, long-term complications of the implant and related-bone are unsolved problems. For the pelvic tumors, the situation is worse.

Methods: Instead of en bloc resection of the tumor-bearing bone, it is just dissected from surrounding normal tissues, then devitalized by hyperthermia in situ. After cleared and re-strengthening the dead bone, its mechanical property becomes strong enough to support the weight bearing.

Results : Between May 1992 and March 2010, 719 patients with malignant bone tumors of the extremities, and 252 patients with malignant pelvic tumors were treated by the novel method. The survival rate: over 3-year survival rate was 59.1% for high-grade malignancy, 88.7% for low-grade malignancy, which is nearly compared with the literature reports, but lower complication rate, better functional outcome, simplified surgical process (especially for the pelvic tumors) should be emphasized.

Conclusion: The applying of hyperthermia for treatment of bone tumors is an effective, simple, and inexpensive method. Hyperthermia should deserve more attention than it has received until now, and should be improved by high tech such as design of antenna, 3D monitoring temperature etc.

E-mail (main author): bonetm@fmmu.edu.cn



O11:104

Recycled autograft augmented with vascularised fibular graft for reconstruction of bone defects caused by tumor resection

Yong-Koo Kang¹, Yang-Guk Chung¹, Won-Jong Bahk¹, An-Hi Lee¹, Jeong-Mi Park¹

¹ The Catholic University of Korea, Republic Of Korea

Recycled autograft for reconstruction of skeletal defect by wide resection for the malignant tumors has been widely used in Asian countries. It has the advantages of using the patients' own bone and providing a good skeletal fit. It has neither donor site morbidity nor risks of disease transmission, and the cost of the treatment is expected to be cheaper comparing to other modalities using mega-prosthesis or allograft.

However, recycled autograft is usually mechanically weak and brittle due to devitalizing process. Heat processing, either autoclaving or pasteurization destroys the BMPs as well, and decreases the mechanical properties. It has been reported a disadvantage of long duration of bone union and high incidences of non-union and fracture. To keep the biologic properties within the recycled bone, it is less processing, and then it increases the risk of the tumor cells survival. Actually, there are a few reports of local recurrences due to tumor cells survival within the recycled autograft in spite of devitalizing process. Thus, confident devitalizing process is mandatory.

To minimize the complications of reconstruction using recycled autograft, it may be augmented with vascularized bone graft. The vascularised fibular graft (VFG) provides the immediate restoration of a physiological blood supply and supplementary stability, and then the cellular elements of the grafts can survive to enhance the bone union and support the strength of the recycled autograft.

We evaluated the outcomes of surgical reconstruction using recycled autograft augmented with VFG for bone defects caused by tumor resections.

Twelve patients with malignant bone tumors who were managed with recycled autograft augmented with VFG and followed up minimum 2 years were evaluated for bone union, functional results and complications. The influence of various factors on bone union and functional outcomes were also analysed. Bone union were obtained at 3.7 months at metaphyseal junctions and 8 months at diaphyseal junctions ($P < 0.05$). At diaphyseal junctions, younger aged group and intramedullary location group showed earlier bone union ($P < 0.05$). The mean functional score was 81%. There were 3 non-unions, 4 delayed unions and 2 recycled bone resorption combined with fractures, although those complications were eventually solved with re-fixation and autogenous bone graft.

In conclusion, recycled autograft for reconstruction should be used for the cases of limited amount of bone destruction, such as tumor contamination of cortical bone due to malignant bone and soft tissue sarcomas.

To obtain excellent results, proper microvascular technique, sufficient length of VFG bridging both junctions, stable internal fixation and proper protection of reconstructed bone until union are necessary.

E-mail (main author): ykang@cmcnu.or.kr



O12:101

Longer Term Follow Up of Compress TKR Fixation

John Healey¹

¹ Memorial Sloan-Kettering Cancer Center, United States

Background: Better, more durable prosthetic fixation is needed. Compliant, compression technology is a novel approach that is being used more frequently with high success rates. This study reports the longest prosthetic follow up to date.

Methods: We retrospectively reviewed the Compress® knee replacement prosthesis in 82 consecutive patients 2000-2008. Twenty-five patients were followed for more than 10 years.

Results: The implants retained fixation in 74 and lost fixation in 8. Kaplan-Meier analysis of the fixation showed five-year survivorship of 85% and 10-year survivorship over 80%. Fixation was lost early in four patients during chemotherapy and had poor bone ingrowth, with lack of bone ingrowth at the interface, crumbling fractures adjacent to the implant and prosthetic failure in 5 patients (Type I). Significant osteonecrosis was found in most patient at the time of autopsy. Fractures developed remote to the implant in three cases (Type IIA), and a unique intercalary fracture (Type IIB) occurred in two patients when there was partial integration of bone into prosthesis. The prostheses were retained in both cases of Type II bone failures. Intramedullary bone formation straddles the spindle mechanism in over half of the cases

Conclusion: Compress fixation has the best survivorship of uncemented distal femoral prostheses, and has unique failure mechanisms.

- Compress fixation is versatile and durable
- 10 year survivorship is 80%
- Novel failure mechanisms were found in these patients
- The significance of Intramedullary bone formation is unknown



O12:102

Reconstruction of massive bone defects using compressive osseointegration

Peter Rose¹, Adam Schwartz¹, Christopher Beauchamp¹, Franklin Sim¹

¹ Mayo Clinic, United States

Background: Extensive segmental bone loss and poor bone quality can complicate revision arthroplasty. Highly porous components, cementless fully-coated stems, and cemented techniques have been described. Unfortunately, these devices can be difficult to remove and may result in even greater bone loss if further revision is needed. Compressive osseointegration has been described as an alternative method to achieve fixation. These devices rely upon compressive initial fixation to achieve biological osseointegration over a comparatively short segment of bone. We believe that compressive osseointegration provides predictable, stable endoprosthesis fixation and that osseointegration can be evaluated radiographically.

Methods: We retrospectively reviewed a total of 34 implants in 30 patients. Procedures were performed at two institutions by six surgeons. Data recorded included patient demographics, indications, diaphyseal segment and joint reconstructed, and any complications. The ratio of total cortex width to spindle width measured at the bone-prosthesis interface on most recent followup AP radiograph was compared to the immediate post-operative ratio measured using the same method. Statistical significance was measured using student's T-test.

Results: 28 of 34 implants (82.4%) achieved stable osseointegration at a mean follow-up of 12.3 months (range 0.5-57.4). The cortex/spindle ratio of these increased from .33 (SD 0.9) postoperatively to .53 (SD 0.15) at latest follow-up ($p < .001$). All reported satisfaction and painless function of the operative limb at latest follow-up. A total of 6 implants in 5 patients failed to achieve stable osseointegration. Cortex/spindle ratio of the failures increased .09, however, this was not statistically significant ($p < .11$). 3 failures were revised using compressive osseointegration; 2 achieved stable fixation. There were no deep infections in this series.

Conclusion: Use of compressive osseointegration for reconstruction of massive diaphyseal and segmental bone defects provides reliable short term fixation, and may prove to be bone conserving in cases that require future re-revision. The cortex/spindle ratio reliably increases as osseointegration is achieved.

E-mail (main author): rose.peter@mayo.edu



O13:101

Allografts versus Iliac Crest Autografts as a Bone Void Filler

William Ward¹, Thomas Rusher¹, Fred Dorey¹

¹ Guthrie Clinic, United States

The senior author began practice in 1991 using iliac crest bone graft almost exclusively as a bone void filler; his practice subsequently evolved into utilizing allograft bone almost exclusively as a bone void filler, creating a unique opportunity to compare the rates of success for the two bone graft types.

We reviewed the surgical case registry of the senior surgeon to identify all cases of bone void filler graft for six benign bone tumors treated over a 20 year period. The charts were reviewed to determine the type of graft utilized, the rates of local recurrence and reoperations for aneurysmal bone cysts, chondroblastomas, enchondromas, non-ossifying fibromas, osteoid osteomas and unicameral bone cysts. All were treated with curettage followed by an iliac crest autograft or an allograft. Allograft types utilized included cancellous allograft (C-Allo), corticocancellous allograft (CC-Allo), or a combination of allografts with cortical strips or struts (Combo); the vast majority of allografts were supplemented with demineralized allograft bone matrix.

Preliminary results (evaluating 331 cases) indicate a tumor recurrence rate of 11.8% (26/221) with allografts compared to 14.6% (16/110, $p=n.s.$) with iliac crest autografts and a reoperation rate for allograft bone grafts of 17.2% (38/221) compared to 23.7% (25/110, $p=n.s.$) in the autograft group. Among the allograft groups, the reoperation rate was 39.1% (9/23) in the Combo group compared to 14.1% (17/121) in the cancellous allograft group and 15.6% (12/77) in the corticocancellous group ($p=0.023$). There was no statistically significant difference in the recurrence rates for the different graft types, but there was a trend for a higher recurrence rate in the Combo group (26.1%, 7/23) that was not statistically different ($p=0.136$). Unicameral bone cysts were the most persistent of the tumor types with more recurrences (24/76, 32%) than any other diagnostic group. None of the enchondromas recurred (0/104, 0%).

These findings demonstrate that for these six entities, allograft bone graft performed as well as autograft. The higher reoperation rate with the Combo allograft group is thought to simply be a reflection of the fact that Combo grafts were used primarily in larger lesions with greater bony compromise. These findings support the continued use of allograft bone graft as a bone void filler for the treatment of the six entities studied.

E-mail (main author): Ward_William@Guthrie.org



O13:102

Improving Outcomes in Soft Tissue Sarcoma with Coordinated Surgery and Intensity Modulated Radiotherapy (IMRT)

Jay Wunder¹¹) Mount Sinai Hospital, Univ. of Toronto, Canada

External-beam radiation is frequently used in the local management of soft tissue sarcomas, but preoperative or postoperative treatment differs substantially in short and long term toxic effects. We previously showed in a randomized clinical trial that preoperative radiation is associated with less long-term radiation morbidity and improved long-term functional benefits for patients with extremity soft tissue sarcoma, but compared to post-operative radiation, is also associated with a higher rate of wound healing complications. We devised a study to determine if a coordinated plan of preoperative image-guided intensity-modulated radiotherapy (IMRT) and surgical resection could reduce morbidity, including wound complications, by minimizing the radiation dose to uninvolved tissues in adults with lower extremity soft tissue sarcoma. The risk of wound healing complications was lowered through the use of IMRT, as was the need for tissue transfer for wound closure and the need for subsequent operations for wound complications. Good limb function, a low risk of long term radiation-related complications, and a low rate of local recurrence were maintained through the use of preoperative IMRT. Implementation of a coordinated plan of image guided IMRT and surgery for extremity soft tissue sarcoma may help minimize the risk and severity of complications, and thereby improve patient outcomes.

E-mail (main author): jwunder@mtsinai.on.ca

O13:103

What's New in Complex Limb Salvage and Reconstructive Procedures

Nicola Fabbri¹¹) Memorial Sloan-Kettering Cancer Center, United States

Surgery remains the most effective treatment for bone and soft tissue sarcomas. Even in the context of multimodal treatment strategy of high-grade lesions, surgical management is crucial and finalized to gain local control of the disease, which remains a fundamental requirement to undertake curative treatment of sarcomas. Surgical margins directly correlate with local control and risk of recurrence. Less than optimal surgical margins and increased risk of local relapse have been historically associated with management of sacropelvic and spine tumors. Today, an integrated multi-dimension surgical imaging system, usually CT based, is available to assist the surgeon with intraoperative "navigation". While intuitively helpful for orientation in a complex three-dimensional anatomy, this exciting opportunity requires clinical validation in terms of achievement of surgical margins, incidence of local recurrence and perioperative complications, and overall cost-effectiveness. Adequate length of follow-up and scientific rigor will be crucial in order to assess these variables and refine indications to intraoperative navigation. Technology is also providing opportunities for improved bone fixation and implant longevity in a variety of different methods. In fact, new foam metal-based implants, have been associated with remarkable bone ingrowth and excellent clinical results, including a post-radiation setting. Improved manufacturing of CT-based, precise-fitting custom implants incorporating porous structure to enhance fixation in critical areas, is also today possible. Interesting appears also the availability on the market of new carbon fiber devices for fracture and prophylactic fixation as an alternative to conventional metal, either stainless steel or titanium. While offering comparable, if not superior, biomechanical properties, carbon fiber-PEEK composite implants are completely radiolucent and associated with essentially no artifacts on CT and MRI imaging. Again, adequate clinical validation is required to fully understand the real impact of these new opportunities in surgery of musculoskeletal tumors.

E-mail (main author): fabbrin@mskcc.org



PSR:101

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

Sebastian Bockholt¹, Arne Streitbürger¹, Georg Gosheger¹, Jendrik Harges¹, Markus Nottrott¹, Marcel-Philipp Henrichs¹, Helmut Ahrens¹

¹Münster University Hospital, Germany

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 none 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 praedominantly 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.

E-mail (main author): SebastianBockholt@gmx.de



PSR:102

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

Frank Traub¹, Dimosthenis Andreou¹, Maya Niethard¹, Carmen Tiedke¹, Mathias Werner¹, Per-Ulf Tunn¹

¹ HELIOS-Klinikum Berlin Buch, Germany

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 (9Ewing's sarcoma, 7 Chondrosarcom, 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.

E-mail (main author): frank.traub@helios-kliniken.de



PSR:103

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

Angelika Schaffler¹, Angelika Schaffler¹, Dimosthenis Andreou², Per-Ulf Tunn², Joanna Szkandera¹, Max Zacherl¹, Andreas Leithner¹

¹ Medical University Graz, Austria ² Helios Klinikum Berlin-Buch, Germany

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.

E-mail (main author): a.j.schaffler@gmail.com



PSR:104

The use of modular Tumourprostheses in the Treatment of skeletal Metastases

Marcel-Philipp Henrichs¹, Arne Streitbürger², Georg Gosheger³, Sebastian Bockholt³, Wiebke Guder³, Markus Nottrott³, Jendrik Harges³

¹ University Hospital Münster ² General Orthopaedics/ Tumourorthopaedics ³ General Orthopaedics / Tumourorthopaedics, Germany

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.

E-mail (main author): marcelphilipp.henrichs@ukmuenster.de



PSR:105

COMPLICATIONS ASSOCIATED WITH THE ARTIFICIAL BONE GRAFT SUBSTITUTE €žGeneX€

Ulrike Pirker-Frühaufl, Jörg Friesenbichler¹, Patrick Sadoghi¹, Werner Maurer-Ertl¹, Christian Weger¹, Koppany Bodo¹, Andreas Leithner¹

¹ Medical University Clinic Graz, Austria

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.

E-mail (main author): pirkerfr@hotmail.com



PSR:106

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

Ajay Puri¹, Ashish Gulia², Manish Pruthi²

¹) Tata Memorial Hospital ²) TMH, India

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.

E-mail (main author): docpuri@gmail.com



PSR:107

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

Stefan Gerger¹, Andreas Leithner², Regina Riedl², Bernadette Liegl-Atzwanger², Beate Rinner²

¹) Medical University of Graz ²) Med. Univ. Graz, Austria

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.

E-mail (main author): stefan.gerger@gmail.com



PSR:108

Laparoscopic assisted resection of an ileosacral chondrosarcoma

G. Ulrich Exner¹, Marc Possover², Plamen Kostov², Kurt Uehlinger¹

¹) orthopaedie zentrum zuerich ²) Possover Center Hirslanden, Switzerland

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.

E-mail (main author): guexner@gmail.com



PSR:109

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

Laura Veneroni¹, Cristina Meazza², Primo Daolio³, Roberto Luksch², Carlo Alfredo Clerici², Stefano Bastoni³, Fabio Giardina³, Graziella Cefalo⁴, Maura Massimino²

¹ University of Milan ² Fondaz IRCCS Istituto Nazionale Tumori ³ C.O.O, Istituto Ortopedico G. Pini, Mila ⁴ Ospedale San Paolo, Milano, Italy

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.

E-mail (main author): laura.veneroni@unimi.it



PSR:110

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

Joanna Szkandera¹, Gudrun Absenger¹, Bernadette Liegl-Atzwanger¹, Martin Pichler¹, Zacherl Maximilian¹, Samonigg Hellmut¹, Stojakovic Tatjana¹, Gerger Armin¹, Andreas Leithner¹

¹ Medical University of Graz, Austria

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.

E-mail (main author): joanna.szkandera@medunigraz.at



T1:101

The way tumor specimens get handled by pathology after the leave the operating theatre

Scott Nelson¹

¹⁾ University of California, United States

Extensive preoperative planning takes place prior to resection of bone and soft tissue tumors. After being removed from the operating theatre, what happens to the tumor often becomes a so called "black box" of unknown events occurring in the pathology laboratory. Understanding that the pathologic examination of the specimen is very important, a discussion of common inadequate as well as proper techniques are discussed, to ensure accurate diagnosis as well as evaluation of surgical margins.

E-mail (main author): SDNelson@mednet.ucla.edu



T1:102

The Molecular Biology of Neoplasms

Shekhar Kumta¹, KC Wong¹, Carol Lau¹, Linda Huang¹

¹⁾ The Chinese University of Hong Kong, Hong Kong

The underlying basis of all neoplasms is a molecular-genetic abnormality that affects the basic cell cycle regulatory mechanism. At a molecular level many sarcomas may be characterized on the basis of their specific molecular aberrations – these include somatic mutations, intergene deletions, gene amplifications, and translocations. Characterization of these tumors based on this signature is expected to improve diagnostic capabilities and provide important predictive and prognostic information.

The cell-cycle related changes that arise as a result of these molecular-genetic aberrations not only explain the patho-physiological changes that arise, but may represent opportunities for specific and targeted therapies.

Molecular markers may help to identify subsets of patient populations that are likely to benefit from a selection of therapeutic choices.

In this presentation we attempt to synthesize currently available knowledge in the context of the altered molecular signaling mechanisms at the cell cycle level that present novel and significant opportunities for understanding the prognosis, treatment choices for sarcomas.



T1:103

Updates on Classification and Grading of Bone and Soft Tissue Tumors

Scott Nelson¹

¹⁾ *University of California, United States*

The most recently published edition of the WHO Classification of Tumors of Bone and Soft Tissue Tumors contains several significant changes that are of importance to both pathologists and treating physicians. The most important updates are discussed.

E-mail (main author): SDNelson@mednet.ucla.edu



T2:101

TRIAL FOR OPTIMAL SURVEILLANCE IN SARCOMAAjay Puri¹, A Gulia²¹) Tata Memorial Hospital ²) TMH, India**Purpose:**

Modern multimodality therapy has improved patient survival ; hence follow-up surveillance strategies are becoming increasingly important with significant clinical and fiscal implications. However, the ideal postoperative protocol vis a vis frequency and appropriate screening modalities for bone and soft tissue sarcomas (BSTS) remains ill-defined.

A prospective randomized controlled trial to evaluate the impact on overall survival of an intensive follow-up protocol (as practiced today) against a more cost effective follow-up protocol in patients operated for extremity BSTS was conducted at our institute.

Method:

Five hundred patients non metastatic at presentation who were operated for primary or recurrent extremity sarcomas (both limb salvage and amputations) were recruited between Jan 2006 and June 2010. They were stratified as (i) Bone or soft tissue sarcomas (ii) High or low grade tumors and (iii) Size < / > 8 cm for bone and < / > 10cm for STS. They were randomised into 4 groups (1)- Intensive 3 monthly follow-up (2) - Intensive 6 monthly follow-up (3) - Cost Effective 3 monthly follow-up (4) - Cost Effective 6 monthly follow-up. The primary end point was overall survival and secondary endpoint was disease free survival (local or distant relapse).

Results:

Early results indicate that increased frequency of surveillance does not seem to significantly impact on either earlier recognition of relapse or overall survival. (DFS p= 0.676, OS p= 0.557). Though increased intensity of surveillance may identify earlier recognition of relapse in bone sarcomas it does not significantly impact on overall survival. (DFS p= 0.012, OS p= 0.555)

Conclusion:

Thus in recurrent sarcomas, it is likely that in the majority of cases the outcome and efficacy of salvage treatment is determined more by inherent tumor biology rather than the treatment itself

E-mail (main author): docpuri@gmail.com



T2:102

The clinical value of pretreatment C-reactive protein in predicting survival of patients with bone sarcoma

Tomoki Nakamura¹, Robert Grimer², Czar Gaston², Munenori Watanuki³, Akihiro Sudo¹, Lee Jeys²

¹ Mie Univ. Graduate School of Medicine, Japan ² The Royal Orthopaedic Hospital, United Kingdom ³ Tohoku Univ. Graduate School of Medicine, Japan

Background: Elevated preoperative serum C-reactive protein (CRP) levels are found in a variety of cancers and an elevated pretreatment CRP level is an indicator of a poorer prognosis in many cancers. Elevated CRP levels have also been shown to be a poor prognostic factor in patients with soft tissue sarcoma. The purpose of this study was to determine whether serum CRP levels before treatment predicted the disease-specific survival and local tumor control in bone sarcoma patients. **Patients:** A total of 318 primary bone sarcoma patients between 2003 and 2010 were retrospectively reviewed at single institution (U.K). Patients that presented with metastases and/or local recurrence at diagnosis were excluded from this study.

Results: Elevated CRP levels were seen in 84 patients. The tumor size, tumor histological grade and tumor stage in the patients with elevated CRP levels were significantly higher than those in patients with normal CRP levels. Patients with elevated CRP levels prior to initial treatment had a poorer disease-specific survival (57% at 5 years) than patients with normal CRP levels (79% at 5 years) ($p < 0.0001$). Patients with elevated CRP levels prior to initial treatment had a poorer local recurrence-free rate (71% at 5 years) after initial treatment than patients with normal CRP levels (79% at 5 years) ($p = 0.04$). Multivariate analysis also showed the preoperative CRP level to be an independent predictor of survival and local control. Individually, pre-treatment CRP levels were prognostic factor for disease free survival in chondrosarcoma and Ewing sarcoma but not osteosarcoma and for local control in osteosarcoma.

Conclusion: Our studies suggested that elevated pretreatment CRP levels may be related to aggressive tumor behavior. We recommend routine measurement of CRP levels in patients with bone sarcoma because this test is familiar to most physicians and is readily accessible.

E-mail (main author): tomoki66@clin.medic.mie-u.ac.jp



T2:103

Post relapse survival in patients with Ewing sarcoma

Stefania Di Girolamo¹, Emanuela Palmerini², Roberto Luksch³, Franca Fagioli⁴, Angela Tamburini⁵, Marilena Cesari², Amelia Tienghi⁶, Abate Massimo², Ferrari Stefano²

¹) Istituto Ortopedico Rizzoli ²) IOR, Bologna ³) INT, Milano ⁴) OIRM, Torino ⁵) Meyer, Firenze ⁶) Oncol. Dept. Ravenna, Italy

Background: Post-relapse survival (PRS) in Ewing sarcoma (EWS) is very poor, with less than 15% probability of survival at 5 years in historical series.

The PRS was evaluated in a selected population of patients with EWS treated according ISG/SSG 3 (non metastatic EWS) and ISG/SSG 4 (metastatic EWS) protocols.

Methods:

EWS patients treated in ISG centers according to ISG/SSG 3 and 4 protocols who relapsed after complete remission (by surgery and/ or radiotherapy) were include into the analysis. Data for the analysis were in part prospectively collected and stored in the ISG database and in part were retrieved from clinical charts.

Results:

Data from 72 ISG/SSG 3 EWS patients and 21 patients who relapsed after completion of ISG/SSG 4 protocols were available for the analysis.

49 (53%) of patients had previously received high-dose chemotherapy (HDCT) with busulfan and melfalan.

Median relapse free interval (RFI) was 16 months in ISG/SSG 3 and 17 months in ISG/SSG 4.

Treatment at 1st relapse was: standard dose chemotherapy in 45 (49.5%) patients; HDCT in 24 (26%); palliative treatment in 19 (20.5%) and surgery only in 5 (5%). Three patients died of treatment-related toxicity.

With a median follow-up of 24 months (1-64), the 3-year post-relapse survival (PRS) was 21% in ISG/SSG 3 and 26% in ISG/SSG 4.

In ISG/SSG 3, 3-year PRS was better for patients with a lung only relapse (48%) and a RFI > 2 years (51%).

3-year PRS was 33% (95%CI 13-54) for patients treated with HDCT and 22% (95%CI 6-39) for those who received standard dose chemotherapy.

Conclusions: Pattern of recurrence and RFI are the main factors influencing PRS in EWS. A 3-years PRS >30% can be expected when HDCT can be given at the time of recurrence.

E-mail (main author): stefania.digirolamo@ior.it



T2:104

Treatment and outcome of soft tissue sarcomas in the elderly and the very elderly: an analysis of 282 patients

P Lechler¹, T Cosker², A Gulati², D Whitwell², H Giele², S Trent², N Athanasou², CLMH Gibbons²

¹Nuffield Orthopaedic Centre ²Oxford Sarcoma Service, United Kingdom

Background

Considering the global phenomenon of population aging, the oncologic treatment and outcome of malignancies in the elderly population is of epidemiological and media interest. There exists little knowledge of the clinical course of the elderly and very elderly patients following the surgical resection of soft tissue sarcomas.

Methods

We retrospectively analysed the clinico-pathologic data of 282 consecutive patients (167 male, 115 female) aged 60 years or above, who were treated operatively for soft tissue sarcomas in a single centre between January 1997 and December 2012. Detailed histological findings, tumour grade, pre-operative staging, operative and adjuvant therapeutic measures, resection margins, recurrence and complications, as well as overall survival rate were documented. Subgroup analysis for the 'elderly' (60 to 80 years, n=225) and the 'very elderly' (≥ 80 years, n=57) was also performed.

Results

The mean age of the elderly subgroup was 69.2 years compared to 84 years in the very elderly patients. At a mean follow up of 55 months (range: 2 to 193), there were no significant differences in the distribution of tumour grade/stage, applied therapeutic measures, complications or recurrence rates between the groups. The most common tumour in either of the groups was liposarcoma. Overall, there were 124 patients with grade I, 43 patients with grade II, and 115 patients with grade III tumours. A total of 33 local recurrences (11.7%) were observed with 26 cases (11.6%) in the elderly group compared to 7 cases (12.3%) in the very elderly ($p>0.05$). Surgical revision for any reason was undertaken in 17.0% patients (n=48), however elderly patients were more likely to receive revision surgery (n=41, 18.2%) compared to the very elderly (n=7, 12.3%). The mean overall survival in the very elderly patients was 64.9% compared to 81.3% in the elderly but when the survival rate was corrected for sarcoma-independent deaths, there was no significant difference between the groups ($p>0.05$).

Conclusion

The results of the present study indicate good to excellent local disease control and overall survival in surgically treated elderly and the very elderly patients with soft tissue sarcomas.

E-mail (main author): phillechler@aol.co.uk



T2:105

Negative prognostic factors in the treatment of Epithelioid Sarcoma

Davide Donati¹, Luca Cevolani¹, Tommaso Frisoni¹, Chaeronlap², Banjobe², Marco Gambarotti¹

¹) Rizzoli, Italy ²) Thailand

Background

Epithelioid Sarcoma (EPS) is a rare malignant tumor involving the distal portion of soft tissue of the limbs. Most of the cases recur involving the nodes leading the patient to death. The aim of the study is to review the Rizzoli series outlining possible negative prognostic factor related to the course of EPS.

Methods

From 1979 to 2007, 44 patients presented with diagnosis of EPS, followed at least 3 years (mean 10, range 3-34) unless premature death. The series include 34 male and 10 female with a mean age of 35 years (range 13-82). Location was the upper limb in 27 patients and the lower in 17, in 33 patients the tumor was distal to the elbow or the popliteal fossa, while in 11 was superior. Thirty-one were classified as normal type an, 9 proximal type; in four cases the pathology material was insufficient for a further classification. The diagnosis was immunohistochemically confirmed testing INI1, vimentin, cytokeratin, CD34 and EMA. In 7 patients antineoplastic chemotherapy and in 17 radiotherapy was associated to surgery.

Results and Conclusion

The overall survival resulted 58%. Ten out of 44 patients with metastasis at presentation died of disease after 24 months average (from 6 to 127). The remaining 34 patients after a mean follow-up of 119 months (range 15-313) resulted with no evidence of disease in 21, in treatment for recurrence of disease in 3 and deceased of disease in 10. Of these 34 patients, 30 received as a first treatment inadequate excision. After the first treatment 16 patients remained free of disease, the other 18 had globally 47 recurrences (range 1-5) and 8 of them ended in amputation. The distal location in the limb had a better prognosis than proximal, while the proximal type had a bad one than the normal type. The use of adjuvant therapies and age didn't show influence for illness course. EPS is a rare soft tissue with high recurrence rate and, inadequate first surgical treatment. Patients with metastasis at presentation, with tumor located proximally in the limb and the histology proximal type resulted with worst prognosis.

E-mail (main author): davide.donati@ior.it



T2:106

Necrosis and vascular invasion identifies high-risk small soft tissue sarcomas

Emelie Styring¹, Linda Hartman¹, Mef Nilbert¹, Pehr Rissler¹, Anders Rydholm¹, Fredrik Vult von Steyern¹

¹Lund University, Sweden

BACKGROUND:

Soft tissue sarcomas (STS) are a heterogeneous group of malignant tumors with varying propensity for metastasis. Overall, small STS (≤ 5 cm) have a good prognosis. There are, however, tumors that do metastasize. We analyzed risk-factors for metastasis in a cohort with small STS in order to investigate if high-risk tumors may be identified at diagnosis and hence may qualify for adjuvant treatment trials.

PATIENT SELECTION:

239 adult patients with ≤ 5 cm STS tumors of extremities or trunk wall were identified in our population-based register. 8 had metastatic disease at diagnosis and 1 patient with localized disease was never operated. 230 patients were included. Uni- and multivariate analysis cox regression analysis were performed to identify risk factors for metastatic disease at 5 years.

RESULTS:

24/230 cases developed metastasis; none with grade 1 or 2 tumors (4-grade system) metastasized and they were therefore excluded from further analysis. In the high grade group the presence of either necrosis or vascular invasion was associated with a 3-fold increased risk of metastatic disease (95% CI 1-7). If both risk factors were present the HR was 11 (95% CI 4-31). Nearly half (8/18) of the patients with tumors revealing both vascular invasion and necrosis developed generalized disease.

DISCUSSION & CONCLUSION:

Necrosis and intratumoral vascular invasion (which can be assessed on routine H&E stainings) have been shown to be prognostic factors in STS in general but have not been investigated specifically in small STS which are considered to have a good prognosis. We found that the presence of tumor necrosis and vascular invasion implied a high risk for metastatic disease also in small sarcomas.

E-mail (main author): emelie.styring@med.lu.se



T2:107

Is death within one year of diagnosis an indicator of delay in presentation for patients with Sarcomas?

Krishna Reddy¹, Rajpal Nandra¹, Robert Grimer¹

¹Royal Orthopaedic Hospital, United Kingdom

The reduction in one-year mortality over the last 20 years in major cancer groups has not been seen in Sarcoma patients. There has been little improvement since the introduction of neo-adjuvantive chemotherapy. It is generally considered that death within one year of cancer diagnosis is related to advanced stage at diagnosis, multiple comorbidities or complications of treatment. Sarcomas can present late with protracted duration of symptoms and large size at diagnosis. This study investigates prognostic factors and whether a delay in presentation affects one-year mortality.

4945 newly diagnosed patients identified from a prospectively recorded, single institution oncology database of which 595 (12%) died within one year. Patients alive at one year reported a longer duration of symptoms compared to those who died (median 24 weeks vs. 20 weeks; $P < 0.020$). Times from referral to diagnosis were comparable. A number of factors have been identified in both soft tissue and osteosarcomas. High histological grade (odds ratio 5.88 $P < 0.001$) and synchronous metastasis (odds ratio 4.71 $P < 0.001$) led to poorer outcomes. Using a Cox-proportional analysis model patient's age, tumour size, metastasis at diagnosis and histological grade were most influential. Where patients died within 1 year, 76% staged TNM 3 or above (HR =4.1).

One-year mortality is easy to measure and well reported. It has now become a proxy for early or late presentation and a performance indicator. It is possible to predict the risk of one-year mortality using factors available at the time of diagnosis. Death within one year does not correlate with a delay in presentation, but is associated with advanced disease at diagnosis.

E-mail (main author): k.reddy@nhs.net



T2:108

Needle biopsy for sarcomas: does local recurrence along the tract really exist?

Michele Boffano¹, Andrea Ferro¹, Ugo Albertini¹, Stefano Marone¹, Elena Boux¹, Andrea Monticelli², Raimondo Piana¹

¹) CTO Hospital ²) University of Torino, Italy

Background

Biopsy is a fundamental step for both the diagnosis and the surgical management of bone and soft tissue sarcomas. It should be performed in a reference centre, even if it is a needle biopsy, but it is unclear whether the tract needs to be excised to prevent recurrences. The aim of the study is to demonstrate the possibility of needle tract recurrence after biopsy.

Methods

Male, 72-year old. Left pelvis osteolysis with soft tissue gluteal involvement. Trephine bone needle biopsy under general anesthesia with diagnosis of G2 chondrosarcoma. En bloc resection and reconstruction with bars and screws were performed with clear wide margins. Biopsy tract was not excised. After 20 months a small subcutaneous lump below the biopsy scar was noticed. A wide excision was performed confirming the diagnosis of chondrosarcoma. A Literature review looking for current strategies in biopsy and needle tract recurrence has been performed.

Results

Considering the papers published in the last 5 years, the current accepted opinion seems to deny the possibility of local recurrence along needle biopsy tract even if the importance of the bioptic act is confirmed. Only 1 out of 5 papers remarked the importance of resecting the biopsy tract in order to prevent local recurrences.

Conclusion

Partially in contrast with recent published papers, this case report confirms the potential local recurrence along the biopsy tract and the necessity to resect it. Further studies possibly related to tumour cell tropism for soft tissues can better stratify the existing recurrence risk in different histotypes.

E-mail (main author): boffano@inwind.it



T3:101

Sarcoma awareness for Junior Doctors – A pilot study

Coonoor Chandrasekar¹, Emily Robinson², Kian Tan³, Emma Illingworth²

¹ Royal Liverpool University Hospital ² RLBHHT ³ MRI, United Kingdom

Introduction and Aims: The Under-Graduate medical curriculum in the United Kingdom does not have a designated module on sarcomas. Hence awareness of sarcomas amongst Junior Doctors is low unless they study in a designated Sarcoma Centre. The aim of the pilot study was to assess the core knowledge about sarcoma amongst Junior Doctors and to assess the increase in knowledge after an online voluntary study module and subsequent questionnaire.

Methods: 105 Junior Doctors were invited to take part. They answered 50 online questions about sarcomas administered through Survey Monkey. They were then provided with four key resources regarding sarcomas to study and they were asked to complete the 50 online questions again. The questions were marked to assess the core knowledge and improvement or otherwise following the provision of sarcoma study resources.

Results: The results of the baseline knowledge test showed that the mean score was 60% [range 28% to 80%]. The results after provision of key sarcoma related resources was 76% [range 58% to 94%]. 85% showed a measureable increase in scores. The average improvement was 16.6% [range 2% to 34%]. The p-value was <0.001, indicating a significant change in score (mean change in score was 6.5 points, 95% CI 3.9pts to 9.2pts).

Conclusions: The pilot study results show that sarcoma awareness could be introduced as a voluntary study module for Junior Doctors with measureable improvement in the knowledge. Increased awareness could help in early detection, appropriate referral, reduction in unplanned excisions and better care for sarcoma patients

E-mail (main author): crc12@hotmail.com



T3:102

Surgical Training – Thinking Outside the Box

Margareta Berg¹

¹) Surgicon Foundation, Sweden

The human anatomy does not differ between countries, cultures or continents. For this simple reason the surgical profession should be the same anywhere on the globe. In reality, surgical training programs are different not only between countries but also within countries. Competition between educational models seems, from this perspective, to be contra-productive. In addition, surgical curriculums will no longer be fixed entities but eternally developing processes, due to the rapid technical development taking place.

Ongoing retirements in surgery, regulated working hours for young surgeons and technical access to surgical simulation systems have created a paradigm shift from time-based to competency-based surgical training. Transformation of a medical student into a skilled surgeon must not take 10 years, and efficient training programs with in-built checkpoints along the process are necessary. In addition, modern surgery requires consistent high quality and documentation, probably by videofilms included in the medical record as the next step.

To create a basis for a global discussion about these topics, the Surgicon Project was launched in 2010, counting the 1st Surgicon Congress in 2011 as its starting point. In three years it has grown into a global informal network engaging world leaders in surgery from the US and Canada to Australia, New Zealand, India, Africa, Turkey, and several European countries. Breaking out one single question has allowed all kinds of organisations and engaged surgeons to take active part in this work, resulting in the 2nd Surgicon Congress, Gothenburg, June 17-19, 2013. Formal decisions might in the future be replaced by more ephemeral but global agreements adopted to new scientific data, as soon as they are published. Modern surgical development requires modern surgical training.

E-mail (main author): congress@surgicon.org



T4:101

New Genetic Characteristics of Chondrosarcoma

John Healey¹

¹ Memorial Sloan-Kettering Cancer Center, United States

Background: Heterozygous mutations of isocitrate dehydrogenase 1 (IDH1) and isocitrate dehydrogenase 2 (IDH2) have recently been identified in cartilaginous neoplasms including conventional central and periosteal cartilage neoplasms. These mutations occur at a single amino acid residue at R132 for IDH1 and R172 and R140 for IDH2. Mutations in these genes lead to impaired ability of IDH1 and IDH2 to catalyze the conversion of isocitrate to alpha ketoglutarate. This results in neomorphic enzymatic activity leading to production of the oncometabolite 2-hydroxyglutarate (2HG). In this study, we analyzed chondrosarcoma for IDH1, IDH2 and other mutations using high-throughput Sequenom-based analysis.

Methods: Chondrosarcomas were genotyped for IDH1 and 2 mutations on the Sequenom Mass Array Platform. In addition, 271 recurrent point mutations across 27 genes were tested as part of the high throughput Sequenom Mass Array Platform panel.

Results: Fifty three chondrosarcomas were selected for the study. There were 30 females and 23 males. The age range was 18 to 77 years with a median of 55 years. Histologically, twenty one (21) were classified as grade I/III, 25 as grade II-III/III and 7 as Dedifferentiated chondrosarcoma. Twenty-six of 53 (50%) patients had mutations in IDH1 or IDH2. No other mutations were detected in the rest of the gene panel (AKT1, AKT2, AKT3, ALK, BRAF, CDK4, CTNNB1, EGFR, ERBB2, FGFR2, FGR3, FLT3, GNAQ, HRAS, JAK2, KIT, KRAS, MAP2K1, MET, NOTCH1, NRAS, PDGFRA, PIK3CA, PIK3R1, PTPN11, RET, SMO) by Sequenom Mass Array spectrometry.

Conclusion:

IDH1 and IDH2 mutations appear to be genetic signatures in half of chondrosarcomas. Downstream effects of these mutations could unravel pathways which could lead to viable therapeutic options. Most common genetic mutations involving genes of the signal transduction pathways do not seem to play a role in the biology of chondrosarcoma.

- Mutations of isocitrate dehydrogenase IDH 1 and IDH 2 occur in one half of chondrosarcomas
- No other candidate genes were mutated in Sequenom analysis.
- Targeting this metabolic pathway promises to be a new strategy to treat chondrosarcoma

E-mail (main author): healeyj@mskcc.org



T4:102

Cancer Stem Cells in Sarcomas

Jay Wunder¹

¹ Mount Sinai Hospital, Univ. of Toronto, Canada

Solid tumors are composed of a heterogeneous population of cells with different in vitro proliferative capacities; only a minority have the ability to initiate tumor formation in immunodeficient mice. This observation led to the concept of cancer stem cells (CSC), which have the ability to self-renew and differentiate. By manipulating these characteristics, CSCs have been postulated to be responsible for driving the growth of tumors and the recurrence of neoplasms after therapy. Although many cancers are maintained by tumor initiating cells (TICs), until recently this had not been demonstrated for mesenchymal tumors, in part due to the lack of unique surface markers that identify mesenchymal progenitors. We previously identified a subpopulation of cells in sarcomas with stem-like or tumor initiating cell (TIC) capacity which can be identified based on a functional biologic assay of their exclusion of Hoechst dye. There was a positive correlation between the percentage of TICs and the grade of the tumour, suggesting a potential prognostic factor. These stem-like cells or TICs preferentially formed tumours upon serial transplantation into immunodeficient mice. Specific signaling pathways appear to be critical for tumour self-renewal as blockade decreases the proportion of stem-like cells and prevents serial transplantation of xenografts. This new data suggests that therapeutically targeting this subpopulation of TICs could be used to improve patient outcome. For undifferentiated pleomorphic sarcoma (UPS), we identified a gene expression signature for TICs that predicts clinical outcome when applied to unsorted patient tumour specimens. This data further supports the clinical relevance of the TIC concept in sarcoma.

E-mail (main author): jwunder@mtsinai.on.ca



T4:103

Enhancement of Structural Bone Allograft Incorporation with Artificial Periosteum containing Autologous Mesenchymal Stem Cells

Yong-Koo Kang¹

¹ St. Vincent's Hospital, Republic Of Korea

Department of Orthopaedic Surgery*, Research Institute of Medical Science+, St. Vincent's Hospital, The Catholic University of Korea.

Purpose: The Purpose of this study was to evaluate the effect of autologous mesenchymal stem cells (MSCs) on structural bone allograft healing.

Methods: Thirty New Zealand white rabbits were divided into two groups. Segmental bone defect was created on the diaphysis of femur, and the defect was reconstructed with structural bone allograft. In experimental group, structural allograft was wrapped around by artificial periosteum(Gelform) containing autologous MSCs, whereas in control group was not containing autologous MSCs. At 4th, 8th, 12th weeks, the femur of rabbits underwent radiographic studies for bone union, and histologic evaluations for bony union with various growth factors. Bone morphogenic protein-2 (BMP-2), BMP-7, vascular endothelial growth factor (VEGF) and receptor activator of nuclear factor-kappa B ligand (RANKL) were measured within the grafted artificial periosteal tissue to evaluate the influence of autologous MSCs on structural bone allograft incorporation.

Results: Bone union was not achieved in both groups at 4th and 8th weeks. At 12th weeks, three out of five femurs in experimental group were united, but no bony union was found in control group. Histologic findings were also confirmed the enhancement of the allograft incorporation in experimental group. All osteogenesis-related factors were increased in experimental group than control group, and the amount was the highest at 4th weeks.

Conclusion: Incorporation of the structural bone allograft could be enhanced if allograft is covered with artificial periosteum containing autologous mesenchymal stem cells.

Key Words: Structural allograft, autologous mesenchymal stem cells, enhancement of bone healing



T4:104

Small molecules and their effect on osteosarcoma cell proliferation

Doris Maugg¹, Jan Smida², Ina Rothenaigner³, Kenji Schorpp³, Kamyar Hadian³, Daniel Baumhoer⁴, Michaela Nathrath⁵

¹) CCG Osteosarcoma ²) CCG OS of HMGU München ³) Toxicology of HMGU München, Germany ⁴) Pathology, University Hospital Basel, Switzerland ⁵) Pediatric Oncology, Klinikum Kassel, Germany

Osteosarcoma (OS) is a pediatric tumor that develops primarily in children and young adolescents. Poor response or resistance to conventional chemotherapy is a major problem in the treatment of this disease.

We here present a screening strategy of small molecule libraries to find new therapeutic drugs that target osteosarcoma and might be applied in addition to conventional treatments. We used automated high-throughput screening to identify compounds out of 25.000s that target OS cell proliferation. Scaled down to 300 compounds that had an effect on cell proliferation, we screened ten different cell lines (osteoblastic cells, various osteosarcoma cell lines and other tumor cell lines) and compared the effects of the selected 300 compounds on cell proliferation.

We observed differences among cell lines in regard to viability after treatment. We further selected by hierarchical clustering compounds that showed the most differential effects on cell proliferation (between 100-25% viability) in the cell lines used. This could exclude non-reproducible hits and so-called frequent hitters. From this cluster, 29 compounds were chosen, that showed high bipolarity, solubility and non-toxic reactive groups. Currently, effects of these compounds are analyzed in more detail. For this, apoptosis induction and alteration of cell morphology and mitochondria are determined as well as structural prediction of potential interaction partners.

Thus, chemical, non-toxic compounds that interfere with cell proliferation in an OS specific or a cancer cell-specific manner might be promising drugs in treatment of osteosarcoma.

E-mail (main author): doris.maugg@helmholtz-muenchen.de



T4:105

Differentially expressed microRNAs in osteosarcoma

Jan Smida¹, Daniel Baumhoer², Kristian Unger³, Kathrin Poos⁴, Eberhard Korsching⁴, Michaela Nathrath⁵

¹) CCG Osteosarcoma, Germany ²) Pathology, University Hospital Basel, Switzerland ³) Rad. Cytogenetics of HMGU, München ⁴) Bioinformatics, University Münster ⁵) Pediatric Oncology, Klinikum Kassel, Germany

Osteosarcomas are genetically complex tumors with abundant structural and numerical alterations. The molecular pathogenesis of the disease is, however, still poorly understood. Besides various oncogenes and tumor suppressor genes, deregulated microRNAs (miRNAs) are known to affect osteosarcoma development and biology. MicroRNA-expression profiling has been recently established as a method to unravel the impact of miRNA-involvement in malignancies in general, whereas deregulation of a single miRNA can have major impact on a multitude of genes.

We investigated six osteosarcoma cell lines for genome-wide miRNA expression and correlated our findings with gene expression profiles to identify biologically active miRNAs. Cultured osteoblasts (hFOB 1.19) and mesenchymal stem cells (L87/4) were used as normal references.

Focussing only on miRNAs that were deregulated in the majority of osteosarcoma cell lines, we identified several miRNAs with oncogenic and tumor suppressor properties, including various members of the oncogenic miR-17-92 cluster. In addition, several genes involved in differentiation, cell cycle control and apoptosis were found be deregulated in osteosarcoma cell lines, most likely due to altered miRNA expression patterns. In order to evaluate these results and to confirm their functional significance in vivo, we analyzed the expression levels of ca 30 miRNAs of interest in a collective of 35 osteosarcoma biopsy samples. We identified several candidate miRNAs that can be used as biomarkers to discriminate responders to chemotherapy and reflecting the metastatic potential in osteosarcoma.

Our findings indicate a crucial impact of deregulated miRNAs with consecutive changes in gene expression in osteosarcomas and strongly suggest pathogenetic and potentially therapeutic implications of miRNA expression.

E-mail (main author): smida@helmholtz-muenchen.de



T4:106

The EGFR Inhibitor Gefitinib Sensitizes Osteosarcoma Cells Against Anthracycline-Based Chemotherapy In Vitro

Florian Sevelda¹, Bernd Kubista¹, Pilipp Theodor Funovics¹, Reinhard Windhager¹, Walter Berger¹

¹Medical University Vienna, Austria

Background:

Hyperactivation of the epidermal growth factor receptor (EGFR) by gene amplification, mutation as well as overexpression is a hallmark of multiple human carcinomas. However, in recent years data have accumulated that EGFR-mediated signals might also contribute to malignant progression and therapy resistance of human sarcomas.

Methods:

Consequently we have investigated if human osteosarcoma cell lines (n=9) express functional EGFR and its useability as therapeutic target. Cytotoxic activity was determined by MTT-assay and clonogenic assay. Changes of downstream pathway proteins were monitored by Western-blotting.

Results:

Osteosarcoma cells expressed distinctly differing level of EGFR reaching in some cases high amounts. However, even low expression levels were sufficient to mediate activation of both MAPK and PI3K pathways (determined by phosphorylation of ERK1/2 and S6, respectively) by EGF exposure in serum-starved cells. The EGFR-specific inhibitor gefitinib completely blocked EGF-mediated and attenuated serum-induced downstream signal activation. While gefitinib applied as single agent demonstrated only limited growth inhibiting activity in short term experiments (72h drug exposure), it led to reduced colony formation in long term experiments in the majority of cell lines. Importantly, gefitinib sensitized EGFR-expressing osteosarcoma cell lines against chemotherapy with doxorubicin and methotrexate, while it antagonised cisplatin-induced cell death.

Conclusion:

Summarizing, our data suggest that EGFR-mediated survival signals protect human osteosarcoma cells against the cytotoxic activity of several antineoplastic drugs. Consequently, combination approaches including EGFR inhibitors in addition to chemotherapy should be evaluated for treatment of high grade osteosarcoma patients.

E-mail (main author): florian.sevelda@meduniwien.ac.at



T5:101

Myxoinflammatory fibroblastic sarcoma: single institution experience and pooled analysis of 138 published cases

Michele Rocca¹, Raffaele Lombardi², Nicola Zanini², Mariacristina Salone², Marco Gambarotti³, Alberto Righi³, Stefania Di Girolamo⁴, Marco Colangeli⁵, Piero Picci⁶

¹ Istituto Ortopedico Rizzoli ² General Surgery Rizzoli Orthopaedic Inst ³ Pathology Dept. Rizzoli Orthopaedic Inst ⁴ Oncology Dept. Rizzoli Orthopaedic Inst ⁵ Orthopaedic Dept Rizzoli Orthopaedic Ins ⁶ Lab of Oncology Rizzoli Orthop Inst, Italy

Myxoinflammatory fibroblastic sarcoma (MIFS) is a rare soft tissue sarcoma first recognized and named at the end of nineties. Since then, only few case reports and small series have been published. It is generally considered a low-grade sarcoma that typically arises in the extremities but large cohorts with long-term follow-up are lacking. The aim of this study is to review our experience and perform a systematic review of published cases focusing on the risk of recurrence.

Database of the Rizzoli Institute was retrospectively queried to identify all patients with a pathological diagnosis of MIFS observed from 1997 to 2012. Similarly, all literature of those years was searched to capture all MIFS reported cases.

Five patients underwent surgery for MIFS in our Institute and 133 cases were found in literature. Not all clinical and pathological data were available for every patient. There were 76 men (55%), median age was 45 years (IQR: 34-56). Median size was 3 cm (IQR: 2-5); the most common sites of presentation were hand (47%) and foot (21%). Pain was present at diagnosis in 14/82 patients (17%) with median symptoms duration before surgery of 7 months (IQR: 3-12). Initial surgery was performed for a suspected benign tumor in 88 patients (74%). Marginal or intralesional resections were reported in 45/71 cases (63%), and re-excision during same hospitalization was performed in 32/45 cases (71%). At a median follow-up of 26 months, a recurrence was observed in 26/118 patients. Median time to recurrence was 15 months (IQR: 7-26). Relapse-free survival (RFS) at 1, 3 and 5 years was 93%, 72% and 67%, respectively. Only symptoms duration less than 7 months was found to be significantly associated with a worse RFS at univariate analysis ($p=0.046$). Metastatic disease was observed in 3 patients (one patient with lymph node metastasis, one patient with metachronous lung metastasis and one patient with synchronous lung metastasis observed at our Institute). MIFS is a rare sarcoma. Clinical findings confirm the "low-grade" nature of MIFS, however, some patients could be affected by aggressive tumour with distant metastases. Extensive preoperative evaluation, wide surgical excision and follow-up are mandatory.

E-mail (main author): michele.rocca@ior.it



T5:102

INFANTILE FIBROSARCOMA - A REPORT FROM THE COOPERATIVE WEICHTEILSARKOM STUDIENGRUPPE

Tobias Dantonello¹, Ivo Leuschner², Christian Vokuhl², Stefanie Kube¹, Niklas Pal³, Felix Niggli⁴, Gustaf Ljungman⁵, Stefan Bielack¹, Ewa Koscielniak¹

¹ Olgahospital, Klinikum Stuttgart ² Dept. of pediatric pathology, Kiel, Germany ³ Karolinska Institutet, Stockholm, Sweden ⁴ University of Zurich, Switzerland ⁵ University of Uppsala, Sweden

Background: Infantile Fibrosarcoma (iFS) is a rare tumour of young children characterized by ETV6-NTRK3 rearrangement. In contrast to fibrosarcoma of adults it carries a much more favourable prognosis. The treatment of choice is either surgical resection, mild chemotherapy or a combination of both. There are however few reports about iFS diagnosed according to current criteria and treated according to the same strategy. The largest published intergroup studies regarding iFS encompass merely 50 patients.

Patients: Fifty-six patients younger than 3 years with iFS from Germany, Sweden, and Switzerland were registered in the consecutive studies of the Cooperative Weichteilsarkom Studiengruppe (CWS) between 1996 and 2010. They were treated according to the same risk-stratification with surgery and/or chemotherapy. The tumor samples were re-reviewed for the purpose of this study.

Results: In 31 patients the diagnosis was confirmed again by immunohistochemistry (Group A) with additional detection of the characteristic rearrangement in n=23/31. All 31 individuals were younger than 6 months at diagnosis, 23/31 were male and 21/31 had their tumor located in the limbs. Merely one patient had primary metastases. Ten patients were treated with surgery alone. The remaining 21 children received chemotherapy with or without surgery. Chemotherapy consisted mainly of vincristine, dactinomycin ± alkylators. In 10 patients the diagnosis was revised at review (Group B). In 15 patients there was no sufficient tumor material available for review (Group C). After a median follow-up of 5 years merely a single child in group A died compared with 4/10 patients in Group B and 3/15 children in Group C. Actuarial 5-year overall survival (OS) for all 56 patients was 86±9%. The outcome of Group A was however significantly better compared with Group B/C (p=0.03).

Conclusion: IFS is a unique soft tissue sarcoma predominantly occurring in the extremities of male infants. Children diagnosed with iFS according to current standards have an excellent prognosis. The detection of the characteristic rearrangement can facilitate the correct diagnosis. Mutilating surgery seems to be rarely necessary. If surgical resection is not simple it can be facilitated or avoided with mild chemotherapy.

E-mail (main author): tobias.dantonello@olgahospital-stuttgart.de



T5:103

Clear Cell Sarcoma of the soft tissues. A retrospective analysis of 35 cases

Giuseppe Bianchi¹, Eric Staals¹, Silvia Campagnoni¹, Davide Donati¹

¹) Istituto Ortopedico Rizzoli, Italy

BACKGROUND: Clear cell sarcoma is a rare soft tissue tumor with a poor prognosis. This lesion shows morphologic similarities to malignant melanoma but has a distinct genetic background. Early diagnosis and initial wide excision are essential for a favourable outcome. The objective of this study is to determine the clinical, pathologic and genetic features of this tumor, in order to recognize it at an earlier stage and improve treatment and prognosis.

METHODS: A retrospective analysis was performed on 35 consecutive cases, treated at the Rizzoli Institute between 1979 and 2009.

RESULTS: There were 19 male and 16 female patients with an age ranging from 8 to 75 years (mean 40 years). Most of the tumors (24) were located in the lower extremity, 8 in the upper extremity and 3 in the trunk. Twenty-five patients (71%) had undergone previous treatments elsewhere. Thirty-one patients (89%) had localized disease at presentation, 2 had lymphnode metastases, one had lung metastases, and one had lung and bone metastases. Half of the tumors was more than 5cm in diameter. All but one patient underwent surgical excision of the tumor. Six patients (18%) underwent an amputation, 28 had limb salvage surgery performed. Surgical margins were inadequate (marginal or intralesional) in 4 cases. Mean follow-up was 64 months (range 0-311 months). Eight patients developed local recurrence, 17 patients had metastatic disease. At last follow-up, 19 patients had no evidence of disease, one patient was alive with disease and 15 patients died of disease. The overall survival rate was 58% at 5 years and 50% at 10-years.

CONCLUSIONS: Clear cell sarcomas are often unrecognized at initial presentation, causing diagnostic delay and inadequate treatments. We believe that early referral to a tertiary centre can improve outcome for patients with clear cell sarcoma. Wide surgical excision is the main treatment, radiotherapy is often used as adjuvant treatment for local control. The role of chemotherapy needs further investigation.

E-mail (main author): giuseppe.bianchi@ior.it



T5:104

Results and prognostic factors in 15 patients with peripheral dedifferentiated chondrosarcoma

Pietro Ruggieri¹, Elisa Pala¹, Eric Henderson², Mohammad Hassani¹, Marco Maraldi¹, Caterina Novella Abati¹, Eugenio Rimondi¹

¹ University of Bologna, Istituto Rizzoli, Italy ² Moffitt Cancer Center, United States

Background: Dedifferentiated chondrosarcoma is an uncommon tumor that is known to arise from pre-existing, low-grade cartilage lesions. Peripheral dedifferentiated chondrosarcomas (PDC) arise from pre-existing exostoses, or extracortically, and may appear as a peripheral chondrosarcoma without the features of its dedifferentiated counterpart. Dedifferentiated chondrosarcoma has a very poor prognosis. Aim of this study was to evaluate the survival of patients with peripheral PDC and to evaluate possible prognostic factors.

Methods: Between 1980 and 2006, 15 patients were treated for PDC: 11 males and 4 females, mean age of 42 years. In 1 case tumor was located in the humerus, in 3 in distal femur, in 1 in emi-anterior chest, in 5 cases in ileums, in 2 in scapula, in 2 proximal femur, in 1 proximal fibula.

The dedifferentiation was in malignant fibrous histiocytoma in 9 cases, osteosarcoma in 5 cases and spindle cell sarcoma in 1 cases. 14 patients received surgery (one patients was not operable for multiple distant metastases): tumor resection in 9 cases, amputation in 5. Chemotherapy was given to 8 patients.

Results: 4 patients (26.6%) were Ned at a mean followup of 14.7 yrs and 11 patients DWD at a mean time of 2.6 yrs. The overall survival of patients was 34% at 10 years. There was not significant difference in survival between patientens with D.C. of the trunk and those with D.C. of the extremities ($p = 0.2397$).

There was no significant difference in survival with chemotherapy and surgery or with surgery only ($p = 0.6269$).

Conclusion: The prognosis for patients with D.C. remains dismal. Surgery with wide margins remains the principal treatment for this condition. There was no statistical evidence of any beneficial effect from chemotherapy.

E-mail (main author): pietro.ruggieri@ior.it



T5:105

Tumors of the foot: epidemiologic analysis and principles of treatment: the Rizzoli Institute experience

Pietro Ruggieri¹, Andrea Angelini¹, Fernando Jorge¹, Giovanni Guerra¹, Elisa Pala¹, Ilaria Piraino¹

¹ University of Bologna, Istituto Rizzoli, Italy

Background: Tumors of the foot are rare. Although most of these are benign, a failure to appreciate their presence may delay diagnosis and treatment. The knowledge of differential diagnosis and an appropriate preoperative planning are the most important factors for adequate treatment.

Aim of this study was to evaluate the incidence, histologic features and treatment strategy of the most common tumors of the foot.

Methods: From 1900 to 2009, 1.170 tumors of the foot were retrospectively analyzed. Imaging included radiographs in all patients, and CT and MRI when available. Diagnosis was established in all cases with biopsy and histologic slides were reviewed. There were 189 and 981 soft tissue and bone lesions, respectively. Localizations were phalanges (240;20%), metatarsal region (245;21%) and hindfoot (685;59%). Benign or pseudotumoral lesions were 870 (74%): multiple chondromas (168), osteoid osteoma (164), solitary osteochondroma (47), Nora disease (78), calcaneal cyst (51), aneurysmal bone cyst (45) were the most frequent lesions observed. Malignant lesions were 300 (26%): Ewing's sarcoma (44), central chondrosarcomas (29), metastatic carcinoma (24) and other more rare entities.

Results: Benign and pseudotumoral lesions are generally treated with curettage with and without bone grafting. Neoadjuvant and adjuvant chemotherapy associated with surgery, is required for responsive malignant lesions. Amputation may be required for tumors involving the hindfoot.

Conclusions: Malignant tumors are relatively rare, but a high level of attention on imaging and clinical examination is required, even when diagnosis seems straightforward. With few exceptions, a biopsy is recommended before proceeding to surgery.

E-mail (main author): pietro.ruggieri@ior.it



T5:106

Malignant bone tumors of the foot – a single-centre analysis of 29 patients

Verena Anna Stockhammer¹, Thomas M. Tiefenboeck², Joannis Panotopoulos¹, Reinhard Windhager¹, Philipp T. Funovics¹

¹ Medical University Vienna ² KH Krems, Austria

Background:

Malignant tumors of the foot are rare and account for 4% of all musculo-skeletal tumors, including any histological tumor entity that also can affect the foot.

Methods:

We analyzed the data of 29 patients with malignant bone tumors of the foot (16 males; 13 females; mean age, 43 years; range, 10-77 years) who were registered within the Vienna Bone and Soft Tissue Tumor Registry since 1963. There were 23 (79%) primary tumors – including 10 (34%) chondrosarcomas, 5 (17%) Ewing's sarcomas, 2 (7%) osteosarcomas, and 6 (21%) others – and 6 (21%) metastases. The phalanges were affected in 7 (24%) patients, the metatarsals in 16 (55%) and the tarsus in 6 (21%) patients. The leading symptoms were swelling (48%) and pain (38%) with a mean duration of 16 months (range, 1-99 months). Surgical treatment consisted of 11 amputations, 4 en bloc resections, 2 ray resections, 2 debulking-procedures and 7 curettages. 3 patients underwent biopsy only. Adjuvant therapy included radiation in 2 patients and chemotherapy in 11 patients.

Results:

Mean follow-up of all patients was 66 months (range, 1-377 months). Surgical complications were encountered in 6 (21%) patients, of whom 3 infections (10%) required revision resulting in one secondary amputation of a toe and one secondary amputation of the foot. No patient with a primary tumor had metastases at the time of diagnosis. Two (7%) patients developed local recurrence after 5 and 10 months after surgery, respectively; both being treated with secondary amputation. One patient developed lung metastasis after 48 months. The respective 10-year overall survival rate of all patients was 63 percent.

Conclusion:

Our results confirm a potential risk for delayed diagnosis of primary malignant tumors of the foot. In case of adequate surgical and – whenever indicated – multidisciplinary treatment, however, oncological results may remain satisfying.

E-mail (main author): verena.stockhammer@meduniwien.ac.at



T6:101

Invasion and metastasis: from basics to real-time imaging

Hiroyuki Tsuchiya¹

¹ Graduate School of Medical Science, Kanazawa University, Japan

Whereas surgical resection and adjuvant therapy can cure well-confined primary tumors, metastatic disease is largely incurable because of its systemic nature and the resistance of disseminated tumor cells to existing therapeutic agents. To overcome metastatic disease, the process how tumor invasion and metastasis happen should be well understood.

Invasion and metastasis are the most insidious and life threatening aspects of cancer. Especially, lung metastasis is a serious condition of the sarcoma patients, which is difficult to treat successfully and directly affects the fate of the patients.

A cell or group of cells must be able to leave the primary tumor, invade the local host tissue, and survive at the secondary sites. This complex process requires the cells to enter into the vascular circulation, arrest at a distant vascular bed, actively extravasate into the metastatic site, and proliferate as a secondary colony. The each step of metastasis is a very complex and dynamic process during which a number of interactions between tumor cells themselves and between tumor cells and the surrounding environment take place. During the past decade, knowledge regarding the molecular and cellular processes involved in the regulation of tumor metastases has dramatically increased through the study of the migration and seeding of cancer cells, tumor–stroma interactions, vascularization of tumors, and gene expression that correlate with metastasis.

To cultivate a better understanding for tumor invasion and metastasis, we have visualized cellular behavior in primary tumors and metastatic site *in vivo*, using fluorescent protein expressing sarcoma cell line. For subcellular imaging, to observe cytoplasmic and nuclear dynamics in the living mouse, cancer cells were labeled in the nucleus with green fluorescent protein and with red fluorescent protein in the cytoplasm. The nuclear and cytoplasmic behavior of cancer cells in real time in blood vessels was imaged as they trafficked by various means or adhered to the vessel surface. During extravasation, real-time dual-color imaging showed that cytoplasmic processes of the cancer cells exited the vessels first, with nuclei following along the cytoplasmic projections. We also observed cancer cells seeding the lungs of live mice in real-time and follow them forming lung metastatic colonies.

Here we first summarize the current knowledge regarding tumor invasion and metastasis cascade. Then we introduce our *in vivo* imaging system and findings from our studies with the use of fluorescent proteins.

E-mail (main author): tsuchi@med.kanazawa-u.ac.jp



T6:102

Surgical treatment of humeral bone metastases - indications and outcome

Dimosthenis Andreou¹, Andreas Frings², Helena Gruja³, Jörg Friesenbichler², Per-Ulf Tunn³, Andreas Leithner²

¹ University Hospital Muenster, Germany ² Medical University of Graz, Austria ³ HELIOS Klinikum Berlin-Buch, Germany

Background: The humerus is the second most common localization of metastases in the long bones. We sought to evaluate the indications and results of various surgical treatment options.

Methods: We retrospectively analyzed the files of 135 patients with actual or impending pathological fractures of the humerus due to bone metastasis of kidney (n=40), lung (n=32), breast cancer (n=26), and other tumors (n=37), who underwent surgical treatment between 1997 and 2011. Mean follow-up was 15 months for all patients (range, 0-117 months) and 27 months for survivors (range, 1-117 months). A two-sample t-test was used to compare means. Fisher's exact test was used to compare unrelated samples. Survival curves were calculated with the Kaplan-Meier method and compared with the log-rank test.

Results: 56 patients underwent endoprosthetic replacement, 45 patients a compound osteosynthesis with a plate and bone cement and 34 patients received an intramedullary nail. There were no significant differences in the duration of surgery between the 3 groups.

Trauma surgeons used significantly more nails, compared to orthopedic oncologists (23/28 vs. 11/107, $p < 0.001$). Intramedullary nailing was performed only in patients with multiple metastases, while 13 of the patients who received an endoprosthesis and 9 of the patients who underwent a compound osteosynthesis had solitary metastases. Patients with lung and breast cancers had a significantly higher probability to receive an intramedullary nail than patients with kidney cancer (12/32 and 12/26 vs. 5/40, $p = 0.009$), who in turn underwent more endoprosthetic replacements (21/40 vs. 11/36 and 5/26, $p = 0.009$). Overall survival amounted to 51% after 1 year and 16% after 3 years. Patients undergoing intramedullary nailing had a significantly worse overall survival after 1 year (24%), compared to those undergoing compound osteosynthesis (56%, $p = 0.007$) and endoprosthetic replacement (64%, $p < 0.001$), probably reflecting the differences in tumor biology and stage of disease. 8 patients suffered from failure of fixation, 4 after intramedullary nailing and 2 each after endoprosthetic replacement and compound osteosynthesis. These differences were not statistically significant.

Conclusion: All of the aforementioned surgical modalities appear to have a low failure rate, provided that the patient's stage and tumor biology are taken into consideration during treatment planning.

E-mail (main author): dimosthenis.andreou@ukmuenster.de



T6:103

A novel approach to predicting survival in patients with symptomatic spinal bone metastases.

Laurens Bollen¹, Yvette Van der Linden¹, Willem Pondaag¹, Marta Fiocco¹, Bas Pattynama¹, Wilco Peul¹, Sander Dijkstra¹

¹LUMC, Netherlands

Background-Extent and type of treatment for symptomatic spinal bone metastases (SBM) should primarily depend on symptoms and secondarily on expected survival time. Predictive models have been developed but their use entails a risk of over- or undertreatment.

Study objective was to develop a new approach to predict survival in patients with symptomatic SBM.

Methods-All patients who were treated for symptomatic SBM between 2001 and 2010 were included in this single center retrospective study (n=1043). Treatment consisted of radiotherapy and/or surgery. Medical records were reviewed for gender (male n=542, female n=501), age (mean 64.8±12.5 years), type of primary cancer, performance status, presence of visceral, brain and bone metastases, number and location of spinal metastases and neurologic functioning. Primary cancers were classified according to Tomita in three categories: slow, medium and fast growing. Performance status was assessed with the Karnofsky performance score (KPS) and neurologic functioning was graded with the Frankel scale. The most prevalent primary tumors were those of breast (n=299), lung (n=250), prostate (n=215) and kidney (n=60). Survival time was calculated as the difference between start of treatment for SBM and date of death. Analysis was performed using the Kaplan-Meier method, univariate log-rank tests and Cox-regression models.

Results-Median follow up duration was 6.6 years and six patients were lost to follow-up. After stratification for primary tumor category, univariate log-rank tests showed an effect of KPS on survival in all three categories (p<0.001). Presence of visceral (p<0.001) and brain metastases (p=0.009) was shown to influence survival only in the slow growth category. Based on these results a flowchart was created, dividing the population in eight groups (figure 1). These groups were matched according to survival, resulting in four categories. Median survival in category A was 31.2 months, followed by 15.4 months for B, 4.8 months for C and 1.6 months for category D (figure 2). Corresponding Hazard ratios were 1.7 (95%CI 1.4-2.2, p<0.001) for B, 4.3 (95%CI 3.4-5.5, p<0.001) for C and 9.1 (95%CI 7.1-11.7, p<0.001) for D.

Conclusion-Assessing patients according to the presented model results in four categories with significantly different survival times. Extent of treatment can be adjusted accordingly.

E-mail (main author): l.bollen@lumc.nl



T6:104

Surgical Treatment of Metastatic Diaphyseal Fracture of the Humerus

Won-Jong Bahk¹, Seung-Koo Rhee¹, Yong-Koo Kang¹, An-Hi Lee¹

¹) The Catholic University of Korea, Republic Of Korea

Introduction: Although there have been a few reports of pathologic fracture of diaphysis of the humerus treated with debulking and internal fixation augmented by polymethylmethacrylate (PMMA), there is only scanty documentation regarding the result of closed interlocking IM nailing. The purpose of our retrospective study is to report the clinical result of closed interlocking intramedullary (IM) nail as well as open reduction with internal fixation augmented by PMMA.

Materials & Methods: 16 cases of 13 patients with pathologic fractures of the humeral diaphysis, who treated with closed interlocking IM nail fixation (Group 1), and 10 patients, who treated with debulking with internal fixation augmented by PMMA (Group 2) between 1998 and 2002 were selected for this study. The clinical records and radiographs were retrospectively reviewed. Pain and function of the upper extremity were each graded as excellent, good, fair or poor using a modification of the rating system of Perez et al.

Results: Group 1; There were 6 male and 7 female with age ranged from 38 to 81 years (aV. 59 years). The follow-up period ranged from 10 weeks to 58 months (aV. 7 months). Main primary cancers include multiple myelomas, lung cancer and breast cancer. The average time of survival after pathologic fracture was 11.7 months. Final results were excellent or good result in 8 cases, fair in 5 cases, and poor in 3 cases. Poor results were related to local tumor progression in 2 lung cancer patients and tumor spread to 5 digits of the ipsilateral hand in a stomach cancer patient. Group 2; There were 6 male and 4 female with age ranged from 46 to 73 years (aV. 58.6 years) The follow-up period ranged from 6 weeks to 35 months (aV. 7 months). Main primary cancers include kidney cancer, lung cancers and adenocancer of unknown origin. The average time of survival after pathologic fracture was 12.6 months. Final results were excellent or good result in 7 patients, fair in 3 patients.

Conclusion; Tumor progression and distant spreading after IM nail insertion were encountered with poor result in patients with lung cancer and stomach cancer but there was no poor result in patient who treated with debulking with internal fixation augmented by PMMA. Therefore although closed interlocking IM is thought to be an excellent option for carefully selected patients particularly with multiple myeloma and breast cancer, patient's functional status before the fracture, life expectancy, type of tumor, local extent of tumor should be comprehensively considered in planning the treatment of metastatic diaphyseal fracture of the humerus.

E-mail (main author): wjbahk@cmc.acuk.ac.kr



T6:105

Surgical procedures for long bone metastases

Oleg Vyrva¹, Yanina Golovina²

¹ Sytenko Institute ² Synenko Institute, Ukraine

Background:

The main goals of surgical procedures for long bone metastases patients are stabilization of impending or established pathological fractures. Surgeon has to decide to perform segmental resection or perform bone stabilization only. It is very important to predict a patient survival value for correct operation.

Methods and Materials:

A review of a prospectively maintained surgical database identified patients for whom surgery was done for long bone metastases. Of these 104 patients, 57 were operated for limb salvage and 47 had not have surgeries because bad general condition. We performed 28 modular endoprosthesis replacement, 16 plate or nail osteosynthesis + bone cementation, 13 palliative intramedullary fixation without segmental bone resection. The most common site of involvement included the proximal femur (41), proximal humerus (25) and distal femur (12). There were renal cell carcinoma (32), lung carcinoma (19) and breast carcinoma (16). We have used method of discriminant analysis for detect a prognostic survival rate of patient with metastatic lesions. Thanks discriminant analysis we could make right indications for different types of surgery.

Results:

Indications for surgery based on patient separation for three survival rate groups. The first group of patients (survivorship till 6 month) with 4 ASA stage (according American Anaesthesiology Scale) with or without pathologic fractures were not operated (47 cases). The first group of patients with 3 ASA stage with pathologic fracture had had an internal fixation only without resection of pathologic bone lesion (13 cases). And the patients from second (survivorship from 6 to 24 month) and third (survivorship longer 2 years) with or without pathologic fractures had had bone metastatic resection and intercalary (plate or nail osteosynthesis + bone cementation) or endoprosthesis replacement (57 cases). Site-specific function was restored and pain controlled for all patients who maintained their limbs.

Conclusion:

The final decision for a certain surgical procedure of metastatic long bone lesions bases on patients survival rate, that could be predict according data of our created computer program and ASA stage. Right selected indications and correct surgery are a low morbidity procedure that provides immediate restoration of function, pain relief, durable stability and better quality of life.

E-mail (main author): vyrva@online.kharkiv.com



T6:106

A novel patient-derived intra-femoral xenograft model of bone metastatic prostate cancer that recapitulates mixed osteolytic and osteoblastic lesions.

Anna A. Kulidjian¹, Omer Raheem¹, Christina Wu¹, Young B. Jeong¹, S. Johanna Melo-Cardenas¹, Tomonori Yamaguchi¹, Kristen M. Smith¹, Daniel Goff¹, Heather Leu¹, Sheldon R. Morris¹, Nicholas A. Cacalano¹, Koichi Masuda¹, Catriona H.M. Jamieson¹, Catriona H.M. Jamieson¹, Christopher J. Kane¹, Christina A.M. Jamieson¹

¹ University of California San Diego, United States

a) Introduction and Objective: Prostate cancer metastasizes to bone in the majority of patients with advanced disease leading to painfully debilitating fractures, spinal compression and rapid decline. Prostate cancer bone metastases often become resistant to therapies including androgen deprivation, radiation and chemotherapy. There are currently few models to elucidate mechanisms of interaction between the bone microenvironment and prostate cancer. It is, thus, essential to develop new patient-derived, orthotopic models. Here we report the development of PCSD1 (Prostate Cancer San Diego 1), a novel patient-derived intra-femoral xenograft model of prostate bone metastatic cancer that recapitulates mixed osteolytic and osteoblastic lesions.

b) Methods: A femoral bone metastasis of prostate cancer was removed during hemiarthroplasty and transplanted into Rag2^{-/-}; μ c^{-/-} mice either intra-femorally or sub-cutaneously. Xenograft tumors were analyzed for prostate cancer biomarker expression using RT-PCR and immunohistochemistry. Osteoblastic, osteolytic and mixed lesion formation was measured using micro-computed tomography (OCT).

c) Results: PCSD1 cells isolated directly from the patient formed tumors in all mice that were transplanted into Rag2^{-/-} mice. Xenograft tumors expressed human prostate specific antigen (PSA) in RT-PCR and immunohistochemical analyses. PCSD1 tumors also expressed AR, NKX3.1, Keratins 8 and 18, and AMACR. Histologic and microCT analyses revealed that intra-femoral PCSD1 xenograft tumors formed mixed osteolytic and osteoblastic lesions. PCSD1 tumors have been serially passaged in mice as xenografts intra-femorally or sub-cutaneously as well as grown in culture. Prostate growth was characterized in 3D co-culture model of the bone niche with human bone marrow derived stromal cells. PCSD1 tumors grew in mice treated with the anti-androgen, bicalutamide, thus, demonstrating castrate resistance with standard of care therapy.

d) Conclusions: PCSD1 xenograft tumors were characterized as advanced, luminal epithelial prostate cancer from a bone metastasis. PCSD1 intra-femoral xenografts formed mixed osteoblastic/osteolytic lesions that closely resembled the bone lesions in the patient. Castration-resistant growth in the bone niche was evaluated in young and aged mice as well as in the presence and absence of novel bone signaling pathway inhibitors. PCSD1 is a new primary prostate cancer bone metastasis-derived xenograft model to study castrate-resistant metastatic disease in the bone and to develop novel therapies for inhibiting prostate cancer growth in the bone- niche.

E-mail (main author): akulidjian@mail.ucsd.edu



T7:101

Spine, sacral & pelvis resections: Reconstruction of bony defect after resection of malignant periacetabular tumor involving the sacroiliac joint

Wei Guo¹

¹ Peking University People's Hospital, China

Objective: Reviewed the patients with malignant periacetabular tumors involving the sacroiliac joint treated surgically in our hospital to assessment of the results of local control and the function of the limb after reconstruction.

Materials and methods: We retrospectively reviewed 21 patients with malignant periacetabular tumor involving the sacrum from July 2002 to July 2010 treated at Peking University People's Hospital. There were 12 female and 9 male patients, with a mean age of 37 years old. The histopathologic diagnosis was chondrosarcoma in 7 patients, Ewing sarcoma in 1 patients, osteosarcoma in 8 patients, malignant giant cell tumor in 1 patient, melanoma in 1 patient and metastatic tumor in 3 patients.

Results: Oncology result: Adequate margins (wide or marginal) were achieved in 12 of 21 (57.1%) patients. Nine patients (9/21, 42.9%) had local relapse, including of 3 of 8 osteosarcoma, 2 of 7 chondrosarcoma, 1 malignant GCT, 1 melanoma and 2 of 3 metastatic tumor. The recurrence rate for tumor-free margins was 25% (3 of 12) and for intralesional margin was 66.7% (6/9). Eight of 9 patients with local recurrence had recurrent lesion at sacral side and 6 of them had intralesional margin at sacral side. All patients were followed up 13 to 59 months, with mean follow-up time 35 months. The lung metastases were found in 5 patients. Seven patients died of diseases, including 4 osteosarcoma, 1 chondrosarcoma, 1 melanoma and 1 metastatic tumor patients. Four patients were alive with disease. Overall survival was 66.7% (14 of 21), and disease free survival was 47.6% (10 of 21).

Functional result: Seventeen of twenty-one patients with bone graft and modular hemipelvic prosthetic reconstruction after resection of the tumor could walk with a crutch 3 months after surgery. The pelvic prosthesis was taken out 6 months after surgery in 1 patient because of deep infection. Average ISOLS function evaluation score was 17, including good in 5, fair in 12 and poor in 4 patients.

Conclusion: Bone graft with resected femoral head and neck on left sacrum and modular hemipelvic prosthetic reconstruction of the bony defect after resection of the periacetabular tumor involving of the sacrum is a good method, by which a reasonable function can be restored in most of the patients.

Key words: Pelvic Tumor, Surgical Resection, Reconstruction

E-mail (main author): bonetumor@163.com



T7:102

Proximal femur and total femur resections

Jendrik Hardes¹

¹) University Clinic of Muenster, Germany

Endoprosthetic replacements of the proximal or total femur are often required in the treatment of patients with primary or secondary bone tumors. Modular tumor prostheses allow a reconstruction of the resulting bone defect. In most cases long-term limb salvage can be achieved. However, local recurrence is much more common in patients with proximal femur tumors in comparison to patients with tumors around the knee and can result in secondary amputation. Also in periprosthetic infection sometimes a secondary amputation cannot be avoided. The most common complication in proximal and total femur replacement is the dislocation of the hip. This presentation summarizes the dislocation rates depending on the different types of articulation (total hip arthroplasty, monopolar or bipolar head) and the methods of capsular reconstruction and soft tissue reattachment. Finally, the functional outcome of patients receiving a proximal or total femur replacement is mentioned.

E-mail (main author): hardes@uni-muenster.de



T7:103

Distal Femur and Proximal Tibia Resections

Nicola Fabbri¹

¹) Memorial Sloan-Kettering Cancer Center, United States

The knee and its proximity is the most common anatomic location requiring surgery for bone sarcomas. Distal femoral and proximal tibia resections are therefore among the most commonly performed limb sparing procedures in Musculoskeletal Oncology. During the last three decades, the indication to limb salvage surgery has greatly expanded because of a favorable combination of factors including new imaging modalities such as CT and MRI scan, introduction of preoperative chemotherapy for high-grade bone sarcomas, and availability of adequate reconstructive options. Careful consideration of tumor location and extension, patient's age, functional demands and expectations, along with family and social support, are key factors to be considered in order to provide optimal treatment customized to each individual patient. The evolution of implant and hinge design, materials, and fixation has substantially improved long term durability and functional outcome of massive prosthetic replacements, while reducing at the same time the incidence of early and late complications. For adult and teen-ager patients, massive prosthesis is the preferred reconstructive technique by most surgeons following distal femoral resection; nevertheless, unicondylar osteoarticular allograft may be considered in selected circumstances after hemiarticular resection. Massive prosthetic replacement and allograft-prosthetic composite are both viable options commonly used for proximal tibia reconstruction. Newer prosthetic designs and novel bone fixation concepts in form of hybrid stemmed-collared and compliant compressive devices are currently associated with excellent mid-term results, as it is also the case for cemented fixation using the French-paradox technique. In pediatric patients, while rotationplasty remains a successful technique predictably associated with durable results, the new generation of non-invasive expandable implants appears significantly improved in both fixation and reliability of closed expansion mechanism.

E-mail (main author): fabbrin@mskcc.org