WELCOME

It is our great pleasure to welcome you to Stuttgart on the occasion of the 22nd EMSOS Conference along with the 10th EMSOS Symposium for Nurses and Allied Health Professionals.

This year's EMSOS conference, held Thursday May 14 and Friday 15 2009 at the Haus der Wirtschaft in downtown Stuttgart, is preceded by an interdisciplinary training course »Bone Tumors in Children and Adolescents« on Wednesday, May 13, and followed by a sarcoma-patient support meeting and meetings of the COSS, CWS, and EURO-E.W.I.N.G. sarcoma groups on Saturday, May 16. We are very pleased to announce that researchers from 32 different countries have submitted a total of over 250 scientific abstracts for presentation at the 2009 EMSOS meeting. In addition, some of Europe's and North America's leading experts have agreed to hold key lectures on a variety of topics relevant to all those with a special interest in bone and soft tissue tumors. Key speakers include Ronnie Barr, Hamilton, CDN, Pancras Hogendoorn, Leiden, NL, Jeremy Whelan, London, UK, Ewa Koscielniak, Stuttgart, DE and Jörg-Thomas Hartmann, Tübingen, DE. We are particularly pleased to announce that Tom DeLaney, Boston, USA, will present the Campanacci Lecture on Proton and Charged Particle Radiotherapy for Challenging Bone and Soft Tissue Sarcomas and Richard Gorlick, New York, USA, the EMSOS Lecture on Current Concepts on the Molecular Biology of Osteosarcoma. Putting a special emphasis on children, adolescents, and young adults, these and other speakers will examine recent advances in the fields of tumor biology, local and systemic treatments for bone and soft-tissue sarcomas, and innovations in quality of life and follow-up programs.

While we fit a lot of scientific content into EMSOS conferences, they are not all work and no play. To get the Stuttgart conference off on the right foot, the EMSOS-Board invites you to join them for a welcome party on Wednesday, 13 May in the excellent »Plenum« restaurant which is based in the parliament building of the German federal state of Baden-Württemberg. On Thursday, 14 May, we hope you will join us for the annual EMSOS gala dinner. This year's dinner has been given the motto »A taste of Stuttgart« and during the evening in what was formerly Germany's largest cooperative wine press you will be able to enjoy some of the best Stuttgart wines, culinary dishes and entertainment. Stuttgart's Lord Mayor, Dr. Wolfgang Schuster, has kindly invited those still in Stuttgart on the evening of Friday 15 May to a drinks reception at Stuttgart's City Hall, following on from which the Allianz Insurance Company has invited us and those attending the national sarcoma survivor meeting organized by the German Childhood Cancer Foundation on the following day to a dinner at their headquarters.

We would like to take this opportunity to extend our special thanks to our sponsors and exhibitors, in particular to our main sponsor Implantcast and our primary sponsors IDM, PharmaMar, and Stryker. Representatives from these and many other companies whose products we use in our clinical work will be available in the industry exhibition to talk to you during the breaks and we encourage you take this opportunity to find out their latest developments and news.

On behalf of the EMSOS-Board and the local organizing committee we wish you an informative, enjoyable and useful conference. We are happy to see so many old friends amongst the list of participants and we look forward to making many new ones.

Yours sincerely

Antonie Taminiau, EMSOS-President; Stefan Bielack, EMSOS-Vice-President and Local Organiser

Thymoglobuline®
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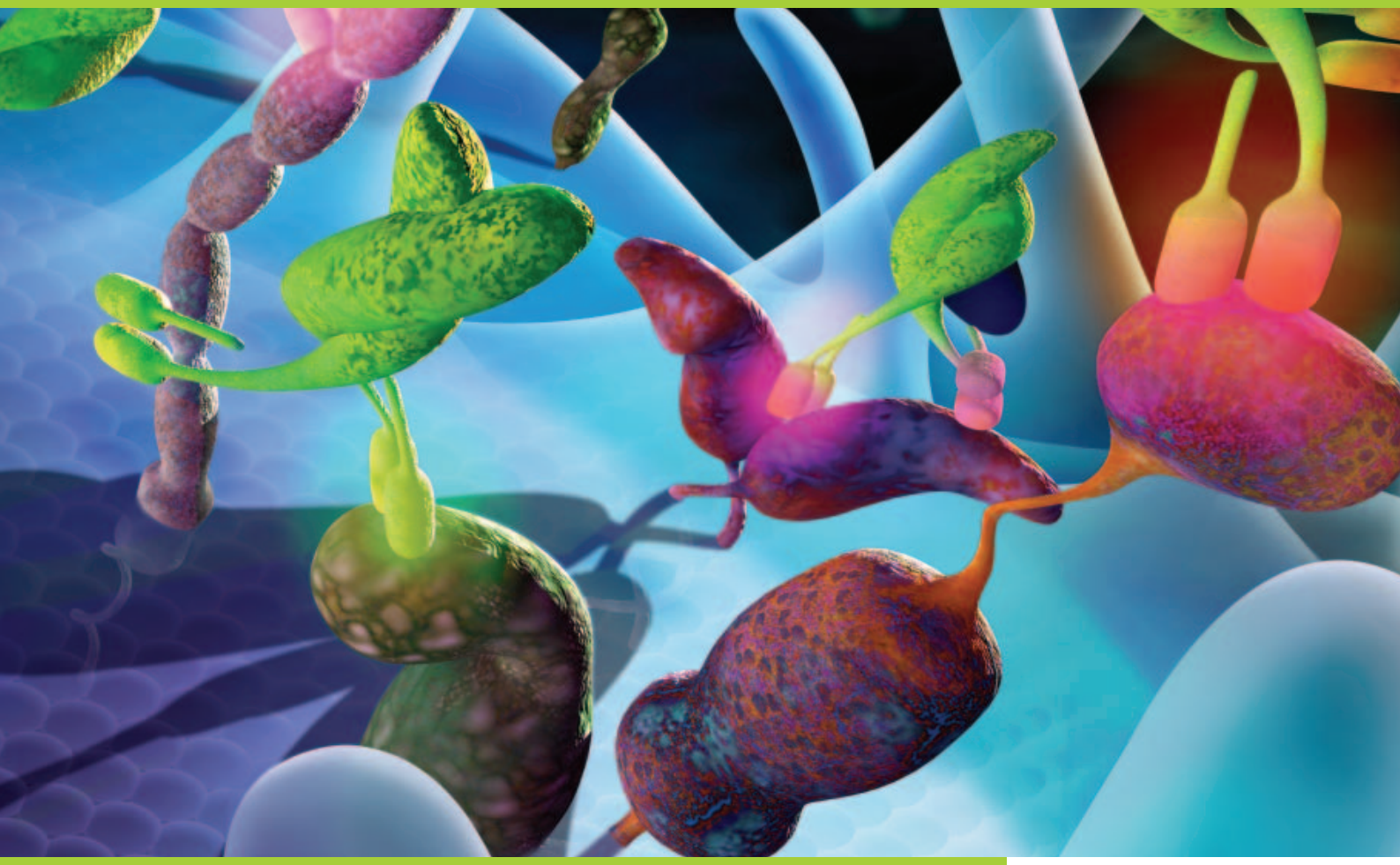

Thymoglobuline
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Thymoglobuline® Pulver für ein Konzentrat zur Herstellung einer Infusionslösung. Wirkstoff: Antihuman T-Zell-Immunglobulin vom Kaninchen. Verschreibungspflichtig. **Zusammensetzung:** Nach Auflösen des Pulvers in 5 ml Wasser für Injektionszwecke enthält 1 ml Lösung 5 mg Antihuman T-Zell-Immunglobulin vom Kaninchen. **Sonst. Bestandteile:** Glycin, Mannitol, Natriumchlorid. **Anwendungsgebiete:** Prophylaxe von Abstoßungskrisen nach Transplantationen von Niere, Herz, Leber und Bauchspeicheldrüse (üblicherweise in Kombination mit anderen Immunsuppressiva); Therapie von Abstoßungskrisen nach Transplantationen von Niere, Herz und Leber; Therapie der aplastischen Anämie, wenn andere Therapien versagen. **Gegenanzeigen:** akute oder chronische Infektionen, Überempfindlichkeit gegenüber Kaninchenproteine oder gegen einen der sonstigen Bestandteile von Thymoglobuline. **Warnhinweis:** Vorsicht bei Vorliegen einer Thrombozytopenie oder Leukozytopenie; ggf. Reaktivierung von Infektionen bei Kombinationsgabe mit anderen Immunsuppressiva sowie erhöhtes Risiko für Krebserkrankungen inkl. Lymphome; mögl. Ausbleiben der Wirkung nach Applikation von Lebendimpfstoffen. Anwendung während Schwangerschaft und Stillzeit nur bei strenger Indikationsstellung. **Nebenwirkungen:** Aus einer Studie: Sehr häufig: reduzierte Anzahl von weißen Blutkörperchen und Blutplättchen, Fieber, Infektionen. Häufig: Durchfall, Schluckbeschwerden, Übelkeit, Erbrechen, Schüttelfrost, Serumkrankheit (Ausschlag, Juckreiz, Gelenkschmerzen, Nierenprobleme, Schwellung der Lymphknoten), Muskelschmerzen, Tumore, Kurzatmigkeit, niedriger Blutdruck. Zusätzliche Meldungen nach Marktzugang: Juckender Ausschlag, Atemprobleme, Magenschmerzen, Schwellungen im Gesicht, der Zunge oder im Hals, pfeifende Atmung oder Husten, Schwindel, Ohnmachtsgefühl, Kopfschmerzen, Blutungen, Blutergüsse, unregelmäßiger oder beschleunigter Herzschlag, Halsschmerzen, Mundgeschwüre. Berichte über das Auftreten von Infektionen, Reaktivierung von Infektionen und Sepsis nach Verabreichung einer Kombination von mehreren Immunsuppressiva. Selten: Tumore und Lymphome. **Hinweis:** Nähere Informationen siehe Fach-/Gebrauchsinformation. **Pharmazeutischer Unternehmer:** Genzyme Europe B.V., Gooimeer 10, 1411 DD Naarden, Niederlande. **Stand:** Juli 2008.

Weitere Informationen erhalten Sie über Genzyme GmbH, Siemensstr.5 b, 63263 Neu-Isenburg, Tel.: +49 (0) 6102 3674-0, Fax +49 (0) 6102 3674-600.

THYMO 3/03-09

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transplantation-info-de@genzyme.com

GENERAL INFORMATION

SCIENTIFIC SESSIONS

Unless otherwise stated, all of the EMSOS scientific sessions will take place in the König-Karl-Halle of the Haus der Wirtschaft. Breaks will take place in the List-Saal, which is also the venue for the poster sessions and industry exhibition. The Nurses and Allied Professionals Symposium will take place in the Karlsruhe Room.

CONTINUING MEDICAL EDUCATION POINTS

The Medical Council of Baden-Wuerttemberg has accredited the training course with 8 points, the EMSOS Conference with 16 points and the GPOH-Research Forum with 6 points. Visit the registration desk to sign the attendance list and pick up your certificate (please note that certificates are only valid if the list has been signed).

The »Arbeitsgemeinschaft Internistische Onkologie« (AIO) has accredited the EMSOS conference with 11 AIO points.

The Nurses and Allied Professionals Symposium is recognized for 9 CME points by the German Society for Voluntary Further Education.

INFORMATION FOR POSTER PRESENTERS

Please have your poster in place in time for the first coffee break and do not take it down until after the final coffee break on Friday afternoon. All authors are expected to be by their poster during their poster session and also to be present during the poster presentations and awards ceremony which will take place during the afternoon of Friday, 15 May. Please note that we are unable to return any posters which are left behind at the end of the conference.

AWARDS CEREMONY

During the awards ceremony which will take place on Friday, 15 May at 16:35 the following prizes, each to the value of 250 Euros, will be awarded:

Best basic science presentation
Best poster presentation
Best oral presentation
Best oral presentation from the Nurses and Allied Professionals Symposium
Best poster presentation from the Nurses and Allied Professionals Symposium.

LUGGAGE

Luggage can be left in the cloakroom of the Haus der Wirtschaft on Friday 15 and Saturday 16 May from 08.00 until the close of the conference.

SECURITY

The Haus der Wirtschaft is a public building with open access to all and no security. We regret that we cannot be held responsible for any loss or damage which might occur to your property during the conference.

INSURANCE

The organisers do not accept liability for individual medical, travel or personal insurance and participants have been advised to make their own arrangements with regards to insurance. The organisers reserve the right to alter or cancel, without prior notice, the conference of any arrangements relating directly or indirectly to it. The organisers shall not be liable for any loss, damage, expenditure or inconvenience caused as result of such alterations or cancellation. The content of this program is correct at the time of publishing. However, the organisers reserve the right to alter or cancel the program if necessary.

PROGRAM OVERVIEW

SESSION	TITLE	TIME/VENUE
	WEDNESDAY, 13.05.2009	
	Training Day on Bone Tumors in Children and Adolescents	08:00 – 18:00 Bertha-Benz Saal
	Welcome party at the Plenum Restaurant	18.30 – 21.00
	THURSDAY, 14.05.2009	
I	**Sarcomas in adolescents and young adults: Treatment as children or as adults?** **Introductory Lecture** Teenagers and young adults with sarcoma – black sheep or just part of the crowd? Jeremy Whelan, London **EMSOS Lecture:** Current concepts on the molecular biology of osteosarcoma Richard Gorlick, New York	Oral: 08:30 - 10:00 König-Karl-Halle Poster: 10:30 – 11:00 List-Saal
2	**European projects: Cross-border sarcoma research** **Key Lecture:** Tumorogenesis in bone Pancras Hogendoorn, Leiden	Oral: 11:00 – 13:00 König-Karl-Halle (no posters)
3	**Rare bone and soft tissue tumors** **Introductory Lectures:** 1. Clear-cell sarcoma – a review of a soft-tissue sarcoma with fatal prognosis; Juergen Bruns, Hamburg 2. Hemangioendotelioma of bone: Does it exist? J.Bovée, Leiden	Oral: 14:00 – 15:45 König-Karl-Halle Poster: 13:00 – 14:00 List-Saal
4	**Long term outcomes** **Introductory Lecture:** Bone and Soft tissue sarcomas: A challenge to the measurement of patient-reported outcomes Ronald D. Barr, Hamilton	Oral: 16:15 - 18:00 König-Karl Halle Poster: 15:45 – 16:15 List-Saal
H	Nurses and Allied Health Professionals	Oral: all day Karlsruhe Room Poster: 13:00 – 14:00 List-Saal
	Transport to the Gala Dinner at the Alte Kelter	18.00 with stop at Arcotel Camino 18:30 direct to venue

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- **Wachstumsprothesen**
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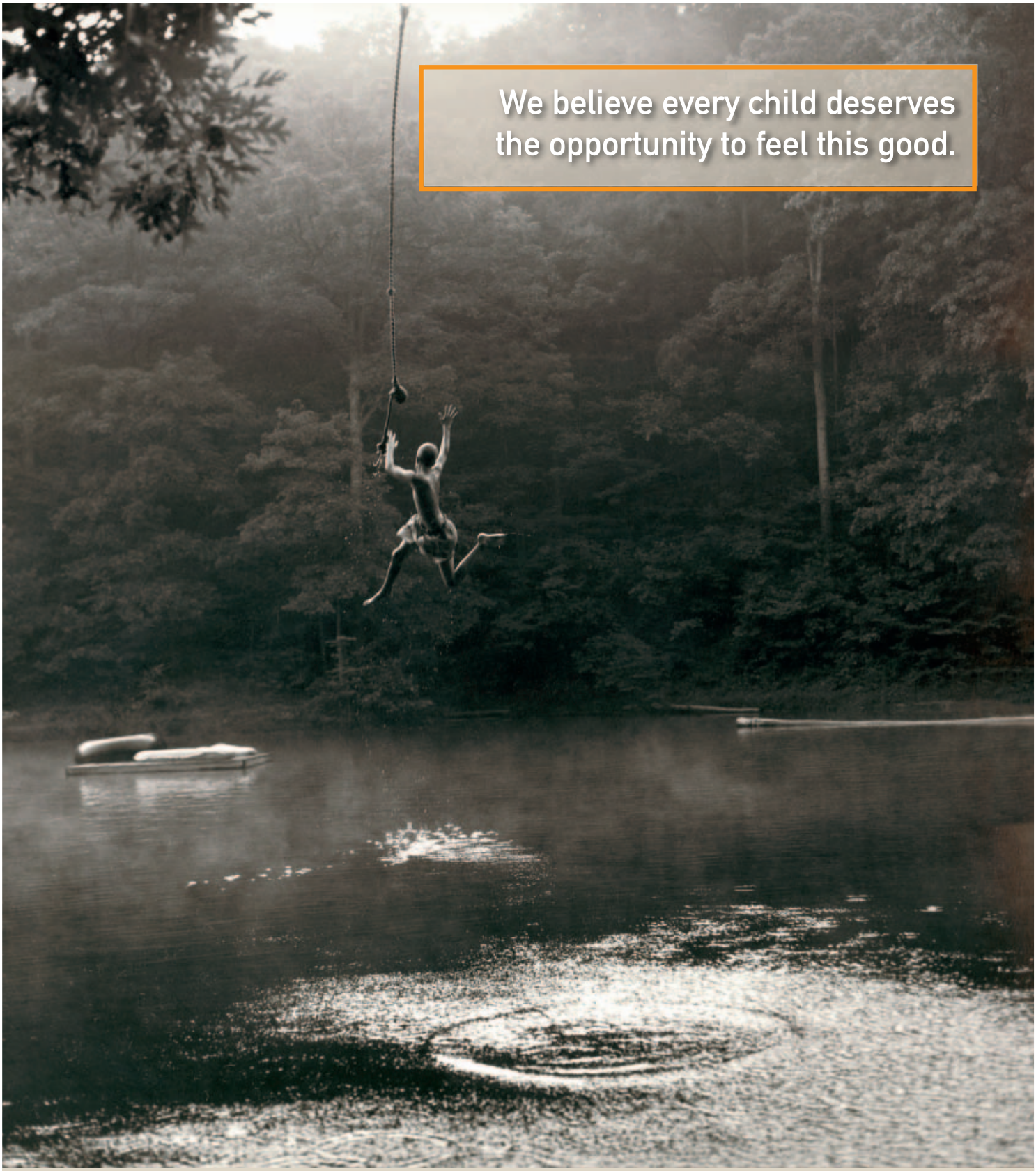
SESSION	TITLE	TIME/VENUE
	FRIDAY, 15.05.2009	
	EMSOS General Assembly, Feedback from the Nurses & Allied Health Professionals	08:00 – 09:00 König-Karl-Halle
	Nurses & Allied Health Professionals Introduction to workshops	08:45 – 09:00 Room Karlsruhe
	Nurses & Allied Health Professionals Workshop 1: Caring for patients in an out-patient environment	Room Karlsruhe
	Nurses & Allied Health Professionals Workshop 2: Caring for wounds after surgery	Studio A
	Nurses & Allied Health Professionals Workshop 3: Dealing with a death on the ward	Studio B
5	Quiz cases	09:00 - 10:00 König-Karl-Halle (no posters)
6	Pediatric soft tissue sarcoma **Introductory Lectures:** 1. Pediatric soft tissue sarcoma as a model for rare tumors: how to intergrate clinical research with clinical practice Ewa Koscielniak, Stuttgart 2. Potential chemotherapy approaches for advanced adult type soft tissue sarcoma Joerg-Thomas Hartmann, Tuebingen	Oral: 10:30 – 12:30 König-Karl-Halle Poster: 10:00 – 10:30 List-Saal
	Nurses & Allied Health Professionals **Summary and close of symposium**	12:30 – 13:00 Room Karlsruhe
	Transport to Factory Outlet Center Metzingen	13:00 From conference venue
7	Mixed free papers **Campanacci Lecture:** Proton and Charged Particle Radiotherapy for Challenging Bone and Soft Tissue Sarcomas Tom DeLaney MD, Boston	Oral: 13:30 –15.15 König-Karl Halle Poster: 12:30 – 13:30 List-Saal
8	Poster Presentations, awards and close of conference	15:45-17:00
	Reception at Stuttgart City Hall followed by dinner at the Allianz Insurance Company	18:00
	SATURDAY, 16.05.2009	
	GPOH Research Forum	09:15 – 16: 45 König-Karl-Halle
	Patients' Support Meeting	09:00 – 16:45 Bertha-Benz Saal



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PHARMA

1ST STUTTGART TRAINING DAY ON BONE TUMORS IN CHILDREN AND ADOLESCENTS

WEDNESDAY, 13 MAY 2009, 08:00 – 18:00

07:00-08:00	REGISTRATION AND COFFEE	
08:00–8:15	Welcome/introduction into the scope of the problem	S. Bielack, Stuttgart, D
	1. Diagnosis and staging	**Moderators: G. Jundt, Basel, CH; J. Treuner, Cairo, Egypt**
	I. Pathology	
08:15-08:35	Histopathology	G. Jundt, Basel, CH
08:35-08:55	Molecular pathology and its interpretation	J. Bovée, Leiden, NL
	II. Imaging and Staging	
08:55-09:15	Radiological techniques (X-Ray, MRI, CT)	T. von Kalle, Stuttgart, D
09:15-09:30	Nuclear medicine (Bone-Scan, PET-CT)	T. Paul, Stuttgart, D
09:30-09:40	Sensitivity and specificity of pulmonary findings	D. Carrle, Stuttgart, D
	III. Biopsy	
09:40-10:00	How to do it right, the consequences of errors on definitive surgery	P. Ruggieri, Bologna, I
10:00 – 10:15	MRI-guided biopsies	T. Wirth, Stuttgart, D
10:15-10:45	BREAK	
	2. Treatment	**Moderators: D. Campanacci, Florence, I; J. Ritter, Münster, D**
10:45-10:55	Interdisciplinary treatment strategies	S. Bielack, Stuttgart, D
	I. Systemic Treatment	
10:55-11:15	Osteosarcoma	J. Whelan, London, UK
11:15-11:35	Ewing's Sarcoma	M. Paulussen, Basel, CH
11:35-11:55	Investigational agents/targeted therapy	S. Ferrari, Bologna, I

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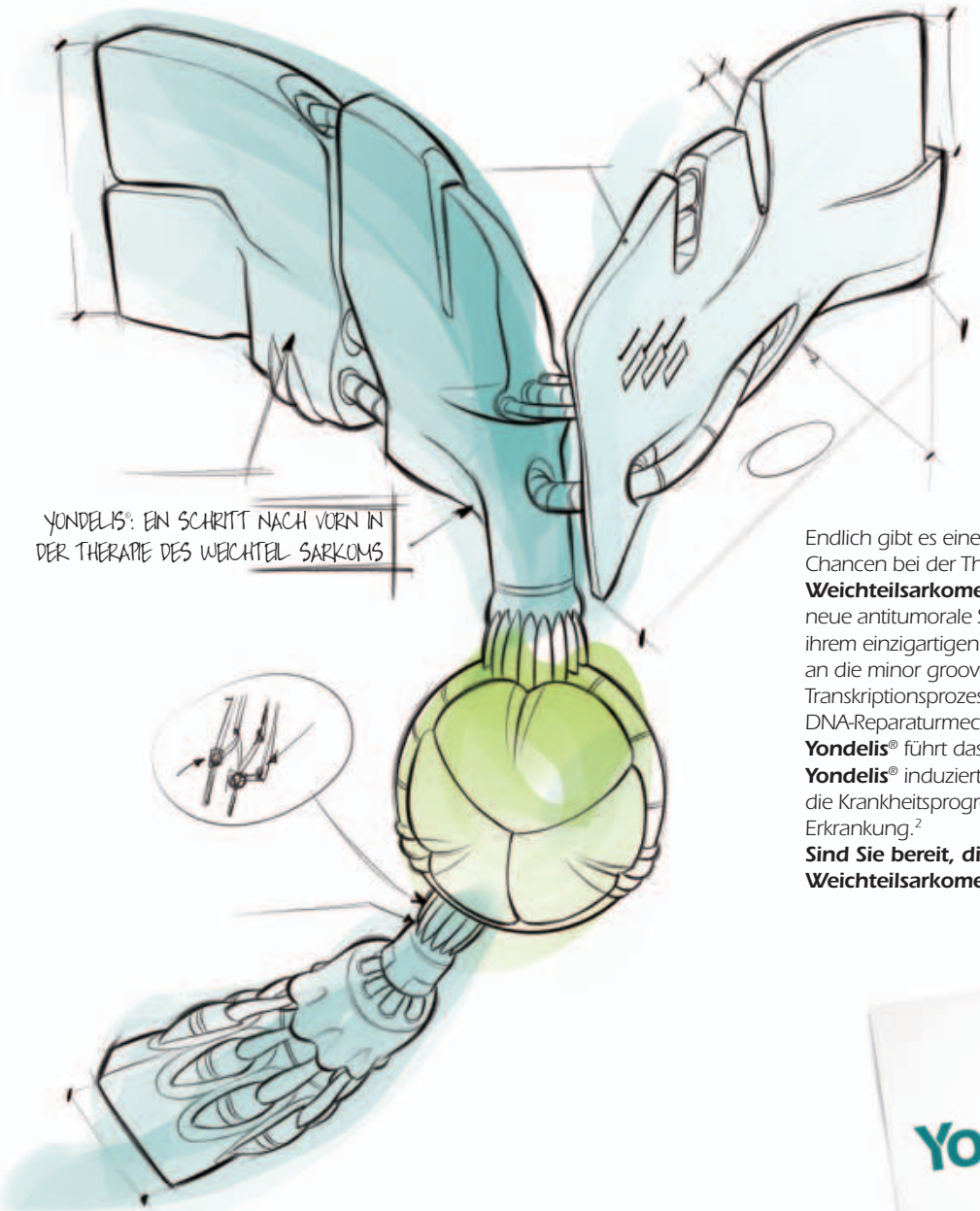

Endlich gibt es eine Alternative, die ganz neue Chancen bei der Therapie von fortgeschrittenen ***Weichteilsarkomen*** *eröffnet:* ***Yondelis®****, die neue antitumorale Substanz aus dem Meer mit ihrem einzigartigen Wirkmechanismus. Sie bindet an die minor groove der DNA und unterbricht Transkriptionsprozesse und DNA-Reparaturmechanismen.*[1]

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Yondelis® ist indiziert zur Behandlung von Patienten mit fortgeschrittenem Weichteilsarkom nach dem Versagen von Anthrazyklinen und Ifosfamid oder von Patienten, bei denen diese Mittel nicht geeignet sind.

März 2009 YON0008-037

Yondelis® 0,25 mg Pulver zur Herstellung eines Infusionslösungskonzentrats **Yondelis® 1 mg** Pulver zur Herstellung eines Infusionslösungskonzentrats **Wirkstoff:** Trabectedin. Zusammensetzung: Jede Durchstechflasche Yondelis® 0,25 mg enthält 0,25 mg Trabectedin, jede Durchstechflasche Yondelis® 1 mg enthält 1 mg Trabectedin. **Sonstige Bestandteile:** Sucrose, Kaliumdihydrogenphosphat, Phosphorsäure und Kaliumhydroxid (zur pH-Anpassung); Yondelis® 0,25 mg enthält 2 mg Kalium und 0,1 g Sucrose, Yondelis® 1 mg enthält 8 mg Kalium und 0,4 g Sucrose je Durchstechflasche. **Anwendungsgebiete:** Behandlung von Patienten mit fortgeschrittenem Weichteilsarkom nach Versagen von Anthrazyklinen und Ifosfamid, bzw. von Patienten, bei denen sich die Anwendung dieser Mittel nicht eignet. Die Wirksamkeitsdaten basieren vorwiegend auf Patienten mit Liposarkom und Leiomyosarkom. **Anwendung:** Zur intravenösen Anwendung nach Rekonstitution und weiterer Verdünnung. Packungsbeilage beachten. Gegenanzeigen: Überempfindlichkeit gegen Trabectedin oder einen der sonstigen Bestandteile. Begleitende schwere oder unkontrollierte Infektion. Stillzeit. Kombinierte Anwendung mit Gelbfiebervakzin CYP3A4 Isoenzym hemmende Medikamente. **Nebenwirkungen:** sehr häufig (≥ 1/10): Erhöhte Kreatininphosphokinase im Blut, erhöhtes Kreatinin im Blut, vermindertes Albumin im Blut, Neutropenie, Thrombozytopenie, Anämie, Leukopenie, Kopfschmerzen, Erbrechen, Übelkeit, Verstopfung, Anorexie, Abgeschlagenheit, Asthenie, Hyperbilirubinämie, erhöhte Alaninaminotransferase, erhöhte Aspartataminotransferase, erhöhte alkalische Phosphatase im Blut, erhöhte Gammaglutamyltransferase. Häufig (≥ 1/100 bis < 1/10): Gewichtsverlust, febrile Neutropenie, periphere sensorische Neuropathie, Geschmacksstörung, Schwindel, Parästhesie, Dyspnoe, Husten, Durchfall, Stomatitis, Bauchschmerzen, Dyspepsie, Schmerzen im Epigastrium, Alopezie, Myalgie, Arthralgie, Rückenschmerzen, Dehydration, Appetitverlust, Hypokaliämie, Infektion, Hypotonie, Flushing (Gesichtsröte), Pyrexie, Ödem, peripheres Ödem, Reaktion an der Injektionsstelle, Insomnie. **Warnhinweise:** Arzneimittel für Kinder unzugänglich aufbewahren. Weitere Informationen siehe Packungsbeilage sowie Fachinformation. Verschreibungspflichtig. **Pharmazeutischer Unternehmer:** Pharma Mar, S.A., Avda. de los Reyes 1, Polígono Industrial La Mina, 28770 Colmenar Viejo (Madrid), Spanien. Yondelis® 0,25 mg, 1 Durchstechflasche, 530 €, Yondelis® 1 mg, 1 Durchstechflasche, 1.994 €. Stand: März 2008.

LITERATUR. 1. Carter NJ, et al. Trabectedin. A review of its use in the management of soft tissue sarcoma and ovarian cancer. Drugs 2007; 67(15): 2257-2276. 2. Morgan JA, et al. Randomized phase II study of trabectedin in patients with liposarcoma and leiomyosarcoma after failure of prior anthracycline and ifosfamide. J Clin Oncol 2007; 25(18S): Abstract 10060.

1ST STUTTGART TRAINING DAY ON BONE TUMORS IN CHILDREN AND ADOLESCENTS

	II. Surgical Resection/Definitive Surgery	
11:55-12:10	Surgical margins & response	P. Picci, Bologna, I
12:10-12:25	Extremity tumors: Surgical options in the growing patient	G. Gosheger, Münster, D
12:25-12:40	Biological reconstruction	D. Campanacci, Florence, I
12:40-12:55	Resection of primaries in non-limb sites	S.D. Dijkstra, Leiden, NL
12:55-13:10	Surgery of (lung) metastases	G. Friedel, Gerlingen, D
13:10-13:30	3. Radiotherapy	A. Schuck, Memmingen, D
13:30-14:30	LUNCH	
	3. Back to normal	**Moderators: T. Alvegård, Lund, SE; M. Paulussen, Basel, CH**
14:30-14:50	Nursing aspects	L. Russell, Birmingham, UK
14:50-15:10	The role of physiotherapy	M. Ekert, Stuttgart, D
15:10-15:30	How the makers of endoprostheses see things	P. Scheinemann, Buxtehude, D
	4. Follow-up and Quality of Life	**Moderators: G. Calaminus, Münster, D, S.D. Dijkstra, Leiden, NL**
15:30-15:50	Tumor-directed follow-up	T. Alvegård, Lund, SE
15:50:16:10	Post treatment convalescence and social care programmes	R. Dopfer, Tannheim, D
16:10-16:30	BREAK	
16:30-16:50	Quality of Life	G. Calaminus, Münster, D
16:50-17:10	What the patients say	R. Heymans, Bonn, D
	5. Problem-based learning, disaster cases	**Moderators: R. Dopfer, Tannheim, D; P. Ruggieri, Bologna, I**
17.10-17:40	· How do disasters come about? · Why a case starts as a disaster but then improves with treatment · How even optimal treatment can end in disasters	R. Grimer, Birmingham, UK
17:40-17:55	Feedback and discussion with members of the EMSOS Board	
17:55-18:00	Farewell	S. Bielack, Stuttgart, D
18:00	WALK TO THE WELCOME PARTY AT THE PLENUM RESTAURANT	

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F-75009 Paris

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216 Boulevard St. Germain
F-75007 Paris

10TH SYMPOSIUM OF THE EMSOS NURSES & ALLIED PROFESSIONALS GROUP

SESSIONS ON THURSDAY 14 MAY, 2009, 08:45 – 18:00

08:00- 08:45	REGISTRATION AND COFFEE	
09:00 – 10:30	**Session 1**	**Moderators: L. Russell, Birmingham, UK, + tbc**
08:45 – 09:00	Welcome	L. Russell, Birmingham, UK; A. Schmid & S. Huether, Stuttgart, Germany
09:00 – 09:30	*Host Lecture:* The changing demands on a paediatric oncology nurse	A. Schmid, Stuttgart, Germany
09:30 – 10:00	*Host Lecture:* The altered self-body image from the patient's perspective and what we need to consider when providing nursing care according to Dorothea Orem	D. Soell, Stuttgart, Germany
10:00 - 10:30	The impact of a bone tumour on the life of a patient: a patient's story	M. Goetze, Stuttgart, Germany
10:30 –11:00	BREAK	
11.00 – 13:00	**Session 2**	**Moderators: H. Sprenger, Stuttgart, Germany, I. Wolfer, Stuttgart, Germany**
11:00 – 11:15	Rotationplasty: guiding patient and family decision making	S.O. Swaim, M.C. Gebhardt; Boston, MA, USA
11:15 – 11:30	Living with Van Nes rotationplasty	N.A.C. Leijerzapf, P.D.S. Dijkstra; A.H.M. Taminiau, Leiden, NL
11:30 – 11:45	Delay in the diagnosis of bone tumours: "Sometimes it's cancer campaign" to improve awareness of cancer symptoms in the teenage and young adult population	S.J. Smith, L. Case, Manchester, UK
11:45 – 12:00	A retrospective study comparing initial GP data on two week wait referrals with clinical review and imaging at a specialist centre	L. Russell, L. Suckling, Birmingham, UK
12:00 – 12:30	*Host Lecture:* The role of postoperative physiotherapy	M. Ekert, Stuttgart, Germany
12:30 – 12:45	United to beat cancer: Physiotherapy and occupational therapy provision on the young oncology unit at the Christie funded by a unique partnership with Manchester United football club	K. Roberts, A. Mann, Manchester, UK

MEDXPERT

MedXpert GmbH – The Chest Wall company.

The mission of the company is to manufacture and distribute two product range of unique quality implants and instruments for the surgical disciplines Pediatric Surgery, Cardiovascular and Thoracic Surgery aiming especially towards chest wall indications:

Pectus Excavatum System (P.E.S.)
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PES is an implant system for the minimally invasive correction of Pectus excavatum. However, in cases with asymmetrical sternal concavities, there is no other option than to correct such deformities in "open" procedures using STRATOS implants for a reliable fixation of the surgical result. Moreover, STRATOS may be used in most cases of chest wall deformities for internal fixation, for stabilization of rib fractures in severe trauma cases and for defect bridging after tumour removal or related reconstructive surgery of chest wall structures.

10TH SYMPOSIUM OF THE EMSOS NURSES & ALLIED PROFESSIONALS GROUP

12.45 – 13:00	The role of the specialist sarcoma physiotherapist in the management of patients with bone and soft tissue sarcoma	L. Richards, M. Cumbo, Manchester, UK
13:00-14:00	LUNCH	
14:00 – 15:45	**Session 3**	**Moderators: N. Leijerzapf, Leiden, NL, S. Berthold, Stuttgart, Germany**
14:00 – 14:30	*Host Lecture:* Evaluating patients' pain and helping with pain-management	Dr. B. Gronwald, Stuttgart, Germany
14:30 – 15:00	*Host Lecture:* Palliative care including a case study based on the Stuttgart, Germany program »HOPPS«	A. Stroehlein, Stuttgart, Germany
15:00 – 15:15	Use of the distress thermometer	G. Egberts, A.C. Biswana, Dr. Jutte; Dr. J. Hoekstra-Weebers, Groningen, NL
15:15 – 15:30	Telephone consult after discharge	D. de Klerk; G. Grootenhuis ten Harkel-Dekker; I.M.S. Heijnen, Nijmegen , NL
15:30 – 15:45	Nurse transfer within the Sarcoma chain	K. Kaesler-te Plate, Nijmegen , NL
15:45 - 16:15	BREAK	
16:15 – 17:30	**Session 4**	**Moderators:, A. Hughes, Birmingham, UK, + tbc.**
16:15 – 16:30	V.A.C.® therapy in surgical wounds	C. Carlos, L. Nancy; M. Rui, S. Dina, Coimbra, Portugal
16:30 – 17:00	*Host Lecture:* Actively managing day-to-day stress on the ward	R. Tellier, Stuttgart, Germany
17:00 – 17:30	Conclusions of the day and look ahead to of the next day	L. Russell, Birmingham, UK A. Schmid & S. Huether, Stuttgart, Germany
18:00	BUS TRANSFER TO ARCOHOTEL CAMINO (THEN AT 18:45 ON TO THE GALA DINNER)	
18:30	BUS TRANSFER DIRECT TO GALA DINNER	

10TH SYMPOSIUM OF THE EMSOS NURSES & ALLIED PROFESSIONALS GROUP

WORKSHOPS ON FRIDAY, 15 MAY, 2009

08:45 – 09:00	Introduction to the workshops Room Karlsruhe	L. Russell, Birmingham, UK; A. Schmid & S. Huether, Stuttgart, Germany
09:00 –11:45	Workshop 1: Caring for patients in an out-patient environment, Room Karlsruhe	I. Wolfer, A. Hermann, K. Coronel, Stuttgart, Germany
09:00 –11:45	Workshop 2: Caring for wounds after surgery Studio A	C. Bodenstein, H. Sprenger, S. Huether, S. Danzer, Stuttgart, Germany
09:00 –11:45	Workshop 3: Dealing with a death on the ward Studio B	S. Heinzmann, K.Roos, Stuttgart, Germany
11:45 – 12:30	Lunch	
12:30 – 13:00	Summary and end of symposium	
13:00	"SHOP UNTIL YOU DROP" - TRANSPORT TO FACTORY OUTLET CENTER METZINGEN	

SCIENTIFIC SESSION 1:
SARCOMAS IN ADOLESCENTS AND YOUNG ADULTS: TREATMENT AS CHILDREN OR AS ADULTS?

Moderators: Stefano Ferarri, Bologna, Italy;
Thomas Klingebiel, Frankfurt/Main, Germany

THURSDAY, 14TH MAY 2009: 08:30 – 10:30
POSTER VIEWING 10:30 – 11:00

TIME	NUMBER	TOPIC	SPEAKER
08:30 – 08:40	-	Opening remarks	A. Taminiau, Leiden, Netherlands; S. Bielack, Stuttgart, Germany
08:40 – 08:55	1 O.01	**INTRODUCTORY LECTURE**	
		TEENAGERS AND YOUNG ADULTS WITH SARCOMA – BLACK SHEEP OR JUST PART OF THE CROWD?	**J. Whelan, London, United Kingdom**
08:55 – 09:05	1 O.02	COMPARING ADULT AND PEDIATRIC RHABDOMYOSARCOMA IN THE SURVEILLANCE, EPIDEMIOLOGY AND END RESULTS PROGRAM, 1973-2005: AN ANALYSIS OF 2600 CASES	I.Sultan, I.Qaddoumi, S.Yaser, C.Rodriguez-Galindo, C.Meazza, M.Casanova, A.Ferrari, Milan, Italy
09:05 – 09:15	1 O.03	TNM STAGING IN EWING SARCOMAS: A MODEL FROM THE (EI)CESS/EE99 STUDIES	H. Jürgens, D. Manner, J. Gerss, A. Ranft, M. Paulussen and U. Dirksen, Münster, Germany
09:15 – 09:25	1 O.04	AN UPFRONT SCORE FOR PRIMARY DISSEMINATED MULTIFOCAL EWING TUMOR PATIENTS PREDICTING OUTCOME - RESULTS FROM THE EURO-E.W.I.N.G. 99 TRIAL	R. Ladenstein, U. Pötschger, M.C. Delay, J. Whelan, M. Paulussen, O. Oberlin, A. Craft, H. Jürgens for the EuroEwing 99 Trial Group, Vienna, Austria
09:25 – 09:35	1 O.05	ONCOLOGICAL OUTCOMES OF PATIENTS WITH EWING'S SARCOMA - IS THERE A DIFFERENCE BETWEEN BONY AND SOFT TISSUE EWING'S SARCOMA?	A. Pradhan, R. J. Grimer, A. Abudu, R. M. Tillman, S. R. Carter and L. Jeys, Birmingham, United Kingdom

TIME	NUMBER	TOPIC	SPEAKER
09:35 – 09.45	1 O.06	IS INSTITUTION A PROGNOSTIC FACTOR IN ADOLESCENT AND YOUNG ADULT PATIENTS WITH OSTEOSARCOMA?	D. Carrle, B. Blank, M. Paulussen, P. Reichardt, S. Bielack, Stuttgart, Germany
09:45 – 09.55	1. O.07	ANEURYSMAL BONE CYSTS – SIMPLE TREATMENT WORKS!	F. Sinnaeve, R.J. Grimer, S.R. Carter, R.M. Tillman, A. Abudu, L. Jeys, Birmingham, United Kingdom
10:00 – 10:30	1. O.08	**EMSOS LECTURE**	
		CURRENT CONCEPTS ON THE MOLECULAR BIOLOGY OF OSTEOSARCOMA	**R. Gorlick, New York, USA**
10:30 – 11:00	Coffee Break **Poster Viewing: Sarcomas in adolescents and young adults: Treatment as children or as adults** Industry Exhibition		

SCIENTIFIC SESSION 2:
EUROPEAN PROJECTS: CROSS-BORDER SARCOMA RESEARCH

Moderators: Judith Bovée, Leiden, The Netherlands;
Hans-Günther Mergenthaler, Stuttgart, Germany

THURSDAY, 14TH MAY 2009: 11:00 – 13:00
(NO POSTERS)

TIME	NUMBER	TOPIC	SPEAKER
11:00 – 11:20	2 O.01	**KEY LECTURE:**	
		TUMOROGENESIS IN BONE	**P. Hogendoorn; Leiden, NL**
11:20 – 11:30	2 O.02	EUROBONET – OSTEOSARCOMA RESEARCH ACROSS THE BORDERS	H. Bürger on behalf of the EuroBoNet consortium; Münster/Paderborn, Germany
11:30 – 11:40	2 O.03	PROGNOSIS AND THERAPEUTIC TARGETS IN THE EWING FAMILY OF TUMOURS - 6TH FRAMEWORK PROGRAM	P. Picci; K. Scotlandi, A. Bernard, F. van Valen, S. Knuutila, A. Llombart-Bosch, H. Kovar, B. Perbal, C. Malvy, M. Gottikh, Bologna, Italy
11:40 – 11:50	2 O.04	CONTICANET: HARMONISING CONNECTIVE TISSUE CANCER RESEARCH AND TREATMENT DEVELOPMENT	J.Y. Blay on behalf of the CONTICANET Network, Lyon, France
11:50 – 12:00	2 O.05	TRANSLATIONAL SARCOMA RESEARCH NETWORK (TranSaRNet)	U. Dirksen, M. Nathrath, K. Agelopoulos, S. Fulda, G. Richer, D. Dilloo, U. Kontny, P. Lang, P. Bader, J.T. Hartmann, E. Korsching, L. Schäfer, S. Bielack, T. Klingebiel, H. Jürgens, Münster, Germany
12:00 – 12:10	2 O.06	ITCC, THE INNOVATIVE THERAPIES FOR CHILDREN WITH CANCER CONSORTIUM: A PARADIGM FOR PAEDIATRIC EARLY DRUG DEVELOPMENT NETWORKS IN EUROPE?	B. Morland, G. Vassal, H. Caron, Birmingham, UK

TIME	NUMBER	TOPIC	SPEAKER
12:10 – 12:20	2 O.07	KIDSCANCERKINOME; KINASE DRUG TARGETS IN PAEDIATRIC CANCERS	H. Caron, G. Vassal, T. Pietsch, O. Delattre, M. Serra, J. Shipley, M. Boer den, S. Clifford, A. Verschuur, R. Versteeg, Amsterdam, The Netherlands
12:20 – 12:30	2 O.08	THE EUROPEAN AND AMERICAN OSTEOSARCOMA STUDY GROUP PROTOCOL, EURAMOS-1: SUCCESSFUL TRANSATLANTIC COOPERATION IN OSTEOSARCOMA	S. Smeland, S. Bielack, M. Sydes, T. Butterfaß-Bahloul, G. Calaminus, N. Marina, M. Tomiczek, J. Whelan, M. Bernstein, Oslo, Norway
12:30 – 12:40	2 O.09	A EUROPEAN TREATMENT PROTOCOL FOR BONE SARCOMA IN PATIENTS OLDER THAN 40 YEARS	S. Ferrari, S. Smeland, S. Bielack, A. Comandone, P. Dileo, P. Picci, K. Sundby Hall, M. Eriksson, H. Honegger, P. Reichardt, Bologna, Italy
12:40 – 12:50	2 O.10	EUROPEAN CLINICAL RESEARCH INFRASTRUCTURES NETWORK (ECRIN) AS A SUPPORT TO MULTINATIONAL TRIALS	J. Demotes-Mainard, Paris, France
12:50 – 13:00	2 O.11	ESF-EMRC FORWARD LOOK INVESTIGATOR-DRIVEN CLINICAL TRIALS: KEY RECOMMENDATIONS FOR STRENGTHENING PATIENT ORIENTED RESEARCH IN EUROPE	C. Moquin-Pattey, Strasbourg, France
13:00 – 14:00	Lunch **Poster Viewing: Rare bone and soft tissue tumors and Nurses & Allied Health Professionals** Industry Exhibition		

SCIENTIFIC SESSION 3:
RARE BONE AND SOFT TISSUE TUMORS

Moderators: Georg Gosheger, Münster, Germany;
Thomas Wirth, Stuttgart, Germany

THURSDAY, 14TH MAY 2009: 14:00 – 15:45
POSTER VIEWING 13:00 – 14:00

TIME	NUMBER	TOPIC	SPEAKER
14:00 – 14:12	3 O.01	**INTRODUCTORY LECTURE 1: CLEAR-CELL SARCOMA - A REVIEW OF A SOFT-TISSUE SARCOMA WITH FATAL PROGNOSIS**	**J. Bruns, Hamburg, Germany**
14:10 – 14:24	3 O.02	**INTRODUCTORY LECTURE 2: HEMANGIOENDOTELIOMA OF BONE: DOES IT EXIST?**	**J. Bovée, Leiden, The Netherlands**
14:24 - 14:33	3 O.03	MOLECULAR AND IMMUNOHISTO-CHEMICAL CHARACTERIZATION OF BONE AND SOFT TISSUE EPITHELIOID HEMANGIOENDOTHELIOMA	A. Parafioriti, S. Del Bianco, E. Armira-glio, P.A. Daolio, S. Mapelli, Milan, Italy
14:33 – 14:42	3 O.04	HEMANGIOENDOTELIOMA OF BONE: A REVIEW OF THE RIZZOLI EXPE-RIENCE	M. Alberghini, P. Ruggieri, A. Angelini, G. Ussia, M. Gambarotti, C. Ferrari, D. Vanel, P. Picci, M. Mercuri, Bologna, Italy
14:42 – 14:51	3 O.05	HIGH-GRADE ANGIOSARCOMA OF BONE: A CLINICOPATHOLOGICAL STUDY OF 64 CASES	S.L.J. Verbeke, F. Bertoni, P. Bacchini, R. Sciot, H.M.H. Kroon, P.C.W. Hogendoo-rn and J.V.M.G. Bovée, Leiden, The Netherlands
14:51 – 15:00	3 O.06	GORHAM SYNDROME IN THE PEL-VIS: CASE REPORT AND LITERATURE REVIEW	C.R. Galia, C.A.S. Macedo, R. Rosito, C.V. Diesel, V. Penna, R.G. Becker, C.A. Pinheiro, E.A. Toller, Porto Alegre, Brazil
15:00 – 15:09	3 O.07	GORHAM-STOUT DISEASE: THE EXPE-RIENCE OF ISTITUTO RIZZOLI	P. Ruggieri, M. Alberghini, M. Montalti, C. N. Abati, L. Zanella, D. Vanel and M. Mercuri, Bologna, Italy

TIME	NUMBER	TOPIC	SPEAKER
15:09 – 15:18	3 O.08	ESTABLISHMENT OF THE CHICK CHORIO-ALLANTOIC MEMBRANE ASSAY FOR GIANT CELL TUMOR OF BONE	M. Balke, A. Neumann, K. Agelopoulos, E. Korsching, J. Hardes, C. Kersting, H. Buerger, G. Gosheger, M. Hagedorn, Münster, Germany
15:18 – 15:27	3 O.09	VIVO AND IN VITRO EFFECTS OF BISPHOSPHONATE TREATMENT ON GIANT CELL TUMOUR OF BONE	C.L.M.H. Gibbons, F. Jones, R. Taylor, H. Knowles, P. Hogendoorn, J.A.H. Wass, M. Balke, C. Gebert, N.A. Athanasou, Oxford, United Kingdom
15:27 – 15:36	3 O.10	INCIDENCE, PREDICTIVE FACTORS AND PROGNOSIS OF CENTRAL CHONDROSARCOMA IN PATIENTS WITH OLLIER DISEASE AND MAFFUCCI SYNDROME; REPORT OF 133 PATIENTS	S.H.M. Verdegaal, J.V.M.G. Bovée, T.C. Pansuriya, R.J. Grimer, B.Toker, P.C. Jutte, D.J.Biau, I.C.M. van der Geest, A. Leithner, A. Streitburger, F.M. Lenke, F.G. Gouin, D.A. Campanacci, P.C.W. Hogendoorn, A.H.M. Taminiau, Leiden, The Netherlands
15:36 – 15:45	3 O.11	EXTRATHORACIC SOLITARY FIBROUS TUMOUR: A RARE ENTITY WITH AN UNPREDICTABLE BEHAVIOUR	E.L. Staals, M. Nogales, M. Alberghini, M. Gambarotti, M. Mercuri, Bologna, Italy
15:45 – 16:15	Break **Poster Viewing: Long-term outcomes** Industry Exhibition		

SCIENTIFIC SESSION 4: LONG TERM OUTCOMES

Moderators: Mikel San Julian, Pamplona, Spain;
Steffan Loff, Stuttgart, Germany

THURSDAY, 14TH MAY 2009: 16:15 – 18:00
POSTER VIEWING: 15:45 – 16:15

TIME	NUMBER	TOPIC	SPEAKER
16:15 – 16:45	4 O.01	**KEY LECTURE:**	
		BONE AND SOFT TISSUE SARCOMAS: A CHALLENGE TO THE MEASUREMENT OF PATIENT-REPORTED OUTCOMES	**R. Barr; Toronto, Canada**
16:45 – 16:55	4 O.02	LONG TERM RESULTS IN KNEE RECONSTRUCTIONS WITH MODULAR UNCEMENTED PROSTHESES FIXED HINGE AFTER RESECTION OF BONE TUMORS: A COMPARISON OF TWO CONSECUTIVE DESIGNS OF THE SAME SYSTEM	P. Ruggieri, E. Pala, C. N. Abati, T. Calabrò, E. Pignotti, M. Montalti, A. Ferraro and M. Mercuri, Bologna, Italy
16:55 – 17:05	4 O.03	LONG-TERM COMPLICATIONS IN PATIENTS TREATED WITH ENDOPROSTHESIS OF LOWER LIMB FOR MALIGNANT BONE TUMORS	P.A. Daolio, S.Bastoni, R. Zorzi, F. Lazzaro, A. Parafioriti, S. Mapelli, Milan, Italy
17:05 – 17:15	4 O.04	INSTABILTY OF THE ENDOPROSTHESIS IN BONE TUMORS. A RETROSPECTIVE ANALYSIS	M.D. Aliev, M.N. Orekhov, S.A. Saravanan, D.V. Nisichenko, P.S. Sergeev, A.A. Babalaev, V.A. Sokolovskiy, Moscow, Russia
17:15 – 17:25	4 O.05	OSTEOARTICULAR ALLOGRAFT RECONSTRUCTION AFTER DISTAL RADIAL RESECTION FOR BONE TUMORS: A SERIES OF 18 CASES AT 1.5 TO 8 YEARS FOLLOW-UP	G. Scoccianti, D.A. Campanacci, G. Beltrami, P. De Biase, P. Caldora, R. Capanna; Firenze, Italy

TIME	NUMBER	TOPIC	SPEAKER
17:25 – 17:35	4 O.06	EXTRA-ARTICULAR BONE- OR SOFT TISSUE TUMOUR RESECTION OF THE KNEE JOINT; RESULTS IN 34 PATIENTS	M. van den Besselaar, S.S. Lim, P.D.S. Dijkstra and A.H.M. Taminiau; Leiden, The Netherlands
17:35 – 17:45	4 O.07	TREATMENT AND OUTCOME OF PAROSTEAL OSTEOSARCOMA - BIOLOGICAL VERSUS ENDOPROSTHETIC RECONSTRUCTION	P.T. Funovics, F. Bucher, R.I. Kotz, M. Dominkus, Vienna, Austria
17:45 – 18:00	4 O.08	LATE SIDE EFFECTS OF NEOADJUVANT CHEMOTHERAPY AND RADIOTHERAPY IN PATIENTS WITH LOCALIZED EWING‘ SARCOMA	A.Longhi, G. Bacci ,C.Ferrari , P.Picci , S.Ferrari, Bologna, Italy
18:00 18:30	Bus transfer to Arcotel (and then at 18:45 on to Gala Dinner) Bus transfer direct to Gala Dinner		

EURAMOS BIOLOGY GROUP (BY INVITATION)
THURSDAY, 14TH MAY 2009: 16:00 – 18:00
Room Freiburg

EMSOS GENERAL ASSEMBLY (FOR MEMBERS ONLY)

Moderator: Antonie Taminiau, Leiden, The Netherlands (EMSOS President)

FRIDAY, 15TH MAY 2009: 08:00 – 09:00

TIME	TOPIC	SPEAKER
8:00	EMSOS General Assembly	A. Taminiau; Leiden, The Netherlands
8:50	Feedback from the Nurses & Allied Health Professionals	L. Russell; Birmingham, United Kingdom

SCIENTIFIC SESSION 5: QUIZ CASES

Moderators: Thor Alvegård, Lund, Sweden;
Peter Winkler, Stuttgart, Germany

FRIDAY, 15TH MAY 2009: 09:00 – 10:00

TIME	TOPIC	PANEL
9:00 – 10:00	Quiz Cases	· M. Greulich, Stuttgart, Germany · P. Reichardt, Bad Saarow, Germany · J. Bramer, Amsterdam, The Netherlands · B. Eisenreich, Stuttgart, Germany
10:00 – 10:30	Coffee Break **Poster Viewing: Pediatric soft tissue sarcoma** Industry Exhibition	

SCIENTIFIC SESSION 6: PEDIATRIC SOFT TISSUE SARCOMA

Moderators: Miklós Szendroi, Budapest, Hungary;
Ewa Koscielniak, Stuttgart, Germany

FRIDAY, 15TH MAY 2009: 10:30 – 12:30
POSTER VIEWING: 10:00 – 10:30

TIME	NUMBER	TOPIC	SPEAKER
10:30 – 10:45	6 O.01	**INTRODUCTORY LECTURE 1: POTENTIAL CHEMOTHERAPY APPROACHES FOR ADVANCED ADULT TYPE SOFT TISSUE SARCOMA**	**J. T. Hartmann; Tübingen, Germany**
10:45 – 11:00	6 O.02	**INTRODUCTORY LECTURE 2: PEDIATRIC SOFT TISSUE SARCOMA AS A MODEL FOR RARE TUMORS: HOW TO INTEGRATE CLINICAL RESEARCH WITH CLINICAL PRACTICE**	**E. Koscielniak, Stuttgart, Germany**
11:00 – 11:10	6 O.03	NO INCREASE OF INCIDENCE RATES OF SOFT TISSUE SARCOMAS IN AUSTRIA - A POPULATION BASED EPIDEMIOLOGIC STUDY AND LITERATURE REVIEW	C.Wibmer, A. Leithner, N. Zielonke, M. Sperl, R. Windhager; Graz, Austria
11:10 – 11:20.	6 O.04	PROGNOSTIC FACTORS AND OUTCOME FOR LOCALIZED EXTREMITYC RHABDOMYOSARCOMA (RMS). THE RESULTS OF A POOLED ANALYZE FROM US AND EUROPEAN COOPERATIVE GROUPS.	O.Oberlin, A.Rey, T. La, G. Bisogno, E. Koscielniak, M. Stevens, W. Meyer, M.Carli, J.Anderson; Villejuif, France
11:20 – 11:30	6 O.05	THE IMPACT OF POOR RESPONSE TO INDUCTION CHEMOTHERAPY ON OUTCOME IN LOCALIZED EMBRYONAL RHABDOMYOSARCOMA. A REPORT FROM THE CWS STUDY GROUP	M. Stark, T.M. Dantonello, P. Winkler, I. Leuschner, T.Bölling, G. Seitz, E. Hallmen, I. Veit-Friedrich, S. Bielack, M. Paulussen, M. Benesch, B. Kazanowska, G. Ljungman, T. Klingebiel, E. Koscielniak; Stuttgart, Germany
11:30 – 11:40	6 O.06	COMPARING CHILDREN AND ADULTS WITH SYNOVIAL SARCOMA IN THE SURVEILLANCE, EPIDEMIOLOGY AND END RESULTS PROGRAM, 1983 TO 2005: AN ANALYSIS OF 1268 PATIENTS	I.Sultan, C.Rodriguez-Galindo, R.Saab, S.Yasir, C.Meazza, M.Casanova, A.Ferrari; Milan, Italy

TIME	NUMBER	TOPIC	SPEAKER
11:40 – 11:50	6 O.07	PROGNOSTIC VALUE OF PAX-FKHR FUSION STATUS IN ALVEOLAR RHABDOMYOSARCOMA: A REPORT FROM THE COOPERATIVE SOFT TISSUE SARCOMA STUDY GROUP (CWS)	S. Stegmaier, E. Aakcha-Rudel, P. Muench, K. Simon-Klingenstein, C. Poremba, K.L. Schaefer, I. Leuschner, B. Kazanowska, A.N. Békássy, C. Int-Veen, E. Hallmen, I. Veit-Friedrich, T.M. Dantonello, S. Bielack, J. Treuner, T. Klingebiel, E. Koscielniak; Stuttgart, Germany
11:50 – 12:00	6 O.08	TARGETING THE P53/HDM2 INTERACTION AS A THERAPEUTIC STRATEGY IN SYNOVIAL SARCOMA	P. Darcy, W. Maruwge, B. Brodin; Stockholm, Sweden
12:00 – 12:10	6 O.09	IDENTIFICATION OF TFE3 AND ASPL/TFE3 FUSION TRANSCRIPTS IN FORMALIN-FIXED, PARAFFIN EMBEDDED TISSUES IN ALVEOLAR SOFT PART SARCOMA (ASPS) - A POWERFUL DIAGNOSTIC TOOL	A. Williams, R.J. Grimer, G. Bartle, V.P. Sumathi, C.M. Mangham, J.M. Meis, L-G. Kindblom; Birmingham, United Kingdom
12:10 – 12:20	6 O.10	SPOT-SCANNING PROTON THERAPY OF SARCOMATOUS TUMOURS IN CHILDHOOD AT PSI	B. Timmermann, C. Ares, A. Staab, T. Bölling, J. Salk, M. Frei, F. Niggli, G. Goitein, E. Hug; Villigen, Switzerland
12:20 – 12:30	6 O.11	PREVALENCE AND RISK FACTORS FOR INADEQUATE SURGICAL RESECTION OF SOFT TISSUE SARCOMAS	F. Gouin, A. Moreau, E. Cassagnau, E. Bompas, D. Waast, F. Lintz; Nantes, France
12:30 – 13:30	Lunch **Poster Viewing: Free papers** Industry Exhibition		

SCIENTIFIC SESSION 7: FREE PAPERS

Moderators: Robert Grimer, London, United Kingdom;
Bernhard Schmidt, Stuttgart, Germany

FRIDAY, 15TH MAY 2009: 13:30 – 15:15
POSTER VIEWING: 12:30 –13:30

TIME	NUMBER	TOPIC	SPEAKER
13:30 – 14:00	7 O.01	**CAMPANACCI LECTURE: PROTON AND CHARGED PARTICLE RADIOTHERAPY FOR CHALLENGING BONE AND SOFT TISSUE SARCOMAS**	**T. DeLaney, Boston, USA**
14:00 – 14:10	7 O.02	KINOME PROFILING OF CHONDROSARCOMA REVEALS SRC-PATHWAY ACTIVITY AND DASATINIB AS OPTION FOR TREATMENT	Y.M. Schrage, I.H. Briaire-de Bruijn, N.F.C.C. de Miranda, A.H.M. Taminiau, T. van Wezel, P.C.W. Hogendoorn, J.V.M.G.Bovée; Leiden, The Netherlands
14:10 – 14:20	7 O.03	RISK PROFILING FOR BONE METASTASIS AND BREAST CANCER: THE INFLUENCE OF THE 1498 C/T POLYMORPHISM OF THE VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF)	H. Clar, P. Krippl, W. Renner, U. Langsenlehner, A. Leithner, G. Gruber, G. Hofmann, B. Yazdani-Biuki, T. Langsenlehner, R. Windhager; Graz, Austria
14:20 – 14:30	7 O.04	EXPRESSION ARRAY ANALYSIS OF OSTEOSARCOMA CELL LINES TO DETERMINE CANDIDATE GENES FOR INVASIVENESS	A. Neumann, E. Korsching, A.M. Cleton-Jansen, R. Duim, H. Bürger, K. Agelopoulos; Münster, Germany
14:30 – 14:40	7 O.05	WHERE IS THE LIMIT OF SILVER-COATINGS AS TOXIC AGENT AGAINST EARLY AND LATE INFECTIONS IN MEGAENDOPROSTHESIS?	H. Ahrens, R. Dieckmann, A. Streitbürger, M. Balke, G. Gosheger, A. Günsel, J. Hardes; Münster, Germany

TIME	NUMBER	TOPIC	SPEAKER
14:40 – 14:50	7 O.06	METABOLIC CHARACTERIZATION WITH (18F)FDG-PET/CT OF LUNG NODULES IN PEDIATRIC OSTEOSARCOMA (OS) AND EWING'S SARCOMA (ES) PATIENTS	M. Berta, A. Cistaro, C. Defilippi, A. Linari, M. Pagano, E. Garrone, A.M. Postini, U. Albertini, M. Mancini, F.Fagioli, A. Brach del Prever; Turin, Italy
14:50 – 15:00	7 O.07	THE INFLUENCE OF SURGICAL AND TUMOUR-RELATED FACTORS ON THE DEVELOPMENT OF LOCAL RECURRENCE IN OSTEOSARCOMA: A RETROSPECTIVE ANALYSIS OF UNSELECTED PATIENTS TREATED ON NEOADJUVANT COOPERATIVE OSTEOSARCOMA STUDY GROUP PROTOCOLS	D. Andreou, S. Bielack, D. Carrle, M. Kevric, S. Fehlberg, R. Kotz, W. Winkelmann, G. Jundt, M. Werner, P. Reichardt, P.U. Tunn; Berlin, Germany
15:00 – 15:10	7 O.08	ZOLEDRONIC ACID AS NEW ADJUVANT THERAPEUTIC AGENT FOR EWING'S SARCOMA	G. Odri, F. Lamoureux, G. Picarda, S. Battaglia, S. Dumoucel, V. Trichet, F. Tirode, K. Laud, S. Burchill, F. Gouin, D. Heymann, F. Rédini; Nantes, France
15:15 – 15:45	Coffee Break **Poster Viewing** Industry Exhibition		

SCIENTIFIC SESSION 8: POSTER PRESENTATIONS

Moderators: Piero Picci, Bologna, Italy;
Alexander Bosse, Stuttgart, Germany

FRIDAY, 15TH MAY 2009: 15:45 – 16:35

TIME	TOPIC	PRESENTER
15:45	Sarcomas in adolescents and young adults	S. Smeland, Oslo, Norway
15:55	Rare bone and soft tissue tumors	M. Mercuri, Bologna, Italy
16:05	Long term outcomes	M. Dominkus, Vienna, Austria
16:15	Pediatric soft tissue sarcoma	J. Fuchs, Tübingen, Germany
16:25	Free papers	J. Casanova, Coimbra, Portugal

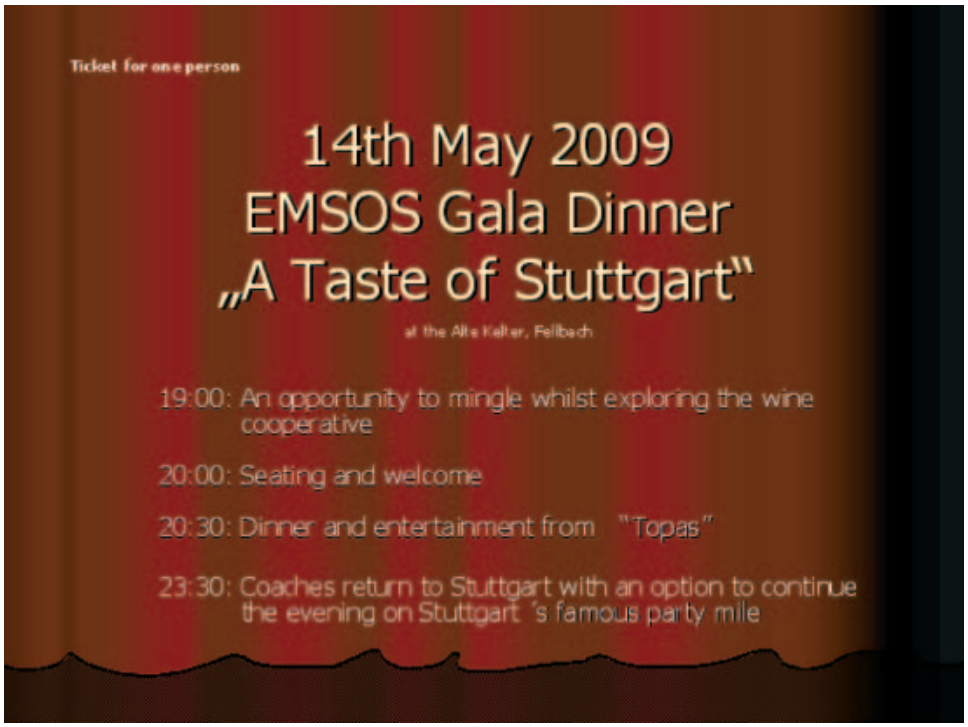
AWARDS CEREMONY

Moderator: S. Bielack, Stuttgart

FRIDAY, 15TH MAY 2009

TIME	TOPIC	PRESENTER
16:35 – 16.50	Award for best basic science presentation	J. Treuner; Cairo, Egypt
	Award for best poster presentation	M. Greulich; Stuttgart, Germany
	Award for best oral presentation	A. Taminiau; Leiden, The Netherlands
	Award for best oral presentation from the Nurses and Allied Professionals' Symposium	M. Goller; Stuttgart, Germany
	Award for best poster from the Nurses and Allied Professionals' Symposium	t.b.c.
16:50 – 17.00	Closing remarks and invitation to EMSOS 2010 in Birmingham, United Kingdom	S. Bielack; Stuttgart, Germany, R. Grimer; Birmingham, UK
17:00	Close of Conference	

DO YOU NEED A TICKET FOR THE GALA DINNER?



Apart from the participants, everything for our evening at the magnificent Alte Kelter (formerly Germany's largest cooperative wine press) has been sourced locally. This includes the flowers on the tables, the beef which will be served as the main course, the award winning wines which come from a vineyard just down the road from the venue, the pralines you will be served with your coffee, and even our entertainer "Topas", who is preparing a show especially for us.

A limited number of tickets (price € 50 per person) are still available. Please ask at the registration desk if you would like to buy one.

EVENING AND SOCIAL EVENTS

WELCOME PARTY

RESTAURANT PLENUM, STUTTGART CITY CENTER
Wednesday, 13 May 2009, 18:30 - 21:00
18:00 Depart Haus der Wirtschaft for the walk to the Plenum Restaurant

EXCURSIONS (1) – »BLOOMING BAROQUE«

Thursday, 14 May 2009
Depart Arcotel Camino (Coach) 09:30, Return circa 16:30

GALA DINNER – »A TASTE OF STUTTGART«

Thursday, 14 May 2009
18:00 Transport from the Haus der Wirtschaft to the Arcotel Camino, then at 18:45 transport to the Alte Kelter
or
18:30 Transport direct from Haus der Wirtschaft to the Alte Kelter
from 23:30 Return to the Arcotel Camino and Stuttgart city center
Please note that entrance to the dinner is by ticket only

SHOP UNTIL YOU DROP

Friday 15 May 2009
13:00 Transport from the Haus der Wirtschaft to Metzingen
16:30 Transport back to Haus der Wirtschaft

RECEPTION AND DINNER

STUTTGART CITY HALL AND ALLIANZ INSURANCE COMPANY
Friday 15 May 2009, Reception: 18:00 - 19:00, Dinner: 19:30
Please note that entrance to these events is by ticket only

EXCURSIONS (2) – »TOYS FOR THE BOYS (AND GIRLS)«

Visit to the MERCEDES BENZ MUSEUM
Saturday, 16 May 2009
Visit to the Mercedes Museum
Transport from Haus der Wirtschaft and Arcotel Camino (Coach) 10:30, Return circa 14:30

INDUSTRY EXHIBITION

The industry exhibition at EMSOS 2009 will take place in the List-Saal and will open during from the first coffee break on Thursday, 14th May until the last coffee break on Friday, 15th May.

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EMSOS 2010 WILL TAKE PLACE IN BIRMINGHAM (ENGLAND), 13/14 MAY 2010

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or contact Rob Grimer by email: rob.grimer@roh.nhs.uk

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The European Musculo-Skeletal Oncology Society was formed in 1987 by a group of Europe's leading orthopedic surgeons, oncologists and other specialists involved in the diagnosis and care of patients with musculoskeletal tumors. Their aim was to provide a forum for the discussion of issues, advances and opportunities which impact on patient survival and care. This is achieved by annual conferences which take place in a different European city in May of each year.

Membership is open to all European clinicians with an interest in bone and soft tissue oncology. There is a membership fee of € 50 and attendance at two EMSOS conferences is a prerequisite. Applications for new membership should be addressed to the Secretary before 30 November prior to the next EMSOS conference and should include:

A letter of recommendation from two members, one from the same country as the applicant, and one from another country.

A curriculum vitae complete with a list of published papers on musculo-skeletal oncology, including reprints of those of major interest.

For further information please speak to one of the EMSOS-Board during the conference or see www.emsos.org

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SATURDAY, 16TH MAY: GPOH RESEARCH FORUM

COOPERATIVE OSTEOSARKOMSTUDIENGRUPPE COSS (IN GERMAN)
EURAMOS-1 PRÜFARZTTREFFEN

SAMSTAG, 16. MAI 2009, 09.15 – 11.15

09.15 – 10.05	EURAMOS1 – Stand der Klinischen Studie	
	Zwischenstand & Amendment	D. Carrle, S. Bielack, COSS-Studienzentrale, Stuttgart
	Pharmakovigilanz	T. Butterfaß-Bahloul, EURAMOS Intergroup Safety Desk, KKS Münster
	Untersuchung zur Lebensqualität	A. Wiener, EURAMOS QoL-Zentrale, Münster
10.05 – 10.15	EURO-B.O.S.S. – Knochensarkome bei 41– bis 65-Jährigen	
	Stand in COSS-Kliniken	S. Bielack, D. Carrle, COSS-Studienzentrale, Stuttgart S. Ferrari, Bologna, P.Reichardt, Bad Saarow
10.15 – 10.55	Projekte unter Nutzung der COSS-Datenbank	
	COSS-Publikationen seit 2006	S. Bielack, Stuttgart
	Solitäre Knochenmetastasen	M. Franke, Stuttgart
	Osteosarkome bei Kindern unter 5 Jahren	L. Kager, Wien
	Radtiotherapie beim Osteosarkom	R. Schwarz, Hamburg
	LESS-Projekte bei COSS-Patienten	T. Langer, Erlangen
10.55 – 11.15	Begleit- und Grundlagenforschung/Zukunftsaussichten	
	Arbeitstreffen Osteosarkom	M. Nathrath, München / Kassel
	Zukunftsaussichten	S. Bielack, Stuttgart
11.15 – 11.45	Break	

COOPERATIVE WEICHTEILSARKOMSTUDIENGRUPPE CWS (IN ENGLISH)

SATURDAY, 16. MAI 2009, 11.45 –14.15

11.45 – 12.00	CWS-2002 P	
	Interim report	T. Dantonello, E.Koscielniak, T. Klingebiel; I. Veit-Friedrich, E. Hallmen CWS Study Group Centre, Stuttgart
12.00 – 12.15	Metastatic soft tissue sarcoma	
	· Interim report CWS-IV-2002 · Information about the upcoming ITCC trial	T. Klingebiel, E.Koscielniak, T. Dantonello, E. Hallmen, I. Veit-Friedrich CWS Study Group Centre, Stuttgart
12.15 – 12.45	Accompanying patho-biological projects	
	Overview	I. Leuschner, Kiel; B. Schäfer, Zürich, Switzerland
	Status report on the minimal disseminated/residual disease project	S. Stegmaier, E. Koscielniak CWS Study Group Centre, Stuttgart
12.45 – 13.15	Break	
13.15 – 14.15	New upcoming projects of the CWS Study Group	
	New structure of the CWS Study Group (registries, guidances, trials, accompanying studies, funding….)	E.Koscielniak, T. Klingebiel, T. Dantonello, E. Hallmen, I. Veit-Friedrich, CWS Study Group Centre, Stuttgart
	Randomized clinical trial CWS-2007-HR	T. Dantonello, E.Koscielniak, T. Klingebiel, I. Veit-Friedrich, E. Hallmen, CWS Study Group Centre, Stuttgart
	Break 15.15 – 15.45	

INITIIERUNG DER NEUEN EWING-STUDIE (BY INVITATION ONLY – IN GERMAN)
SAMSTAG, 16. MAI 2009, 14:15 – 16:45

Darstellung der Studie	Uta Dirksen, Heribert Jürgens
SAE Management	ZKS Münster
Monitoring	ZKS Münster
ICH Guideline for Good Clinical Practice	ZKS Münster
Datenmanagement, Dokumentation	Susanne Amler, Andreas Ranft
Diskussion	

PATIENTS' SUPPORT MEETING (IN GERMAN)
SAMSTAG, 16. MAI 2009, 9:00 – 17:00

This full day of workshops and symposia covering all aspects of sarcoma in children and adolescents is open to patients, their families, carers and those providing services to patients and carers, including nurses and other front-line medical staff.

Using a combination of lectures, symposia and practical sessions, participants will have an opportunity to mix and share experiences with fellow sufferers and leading experts. This meeting is organized by the German Childhood Cancer Foundation and all lectures and workshops will take place in German.

For further information please see *www.kinderkrebsstiftung.de*

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ABSTRACTS

1.O.01

TEENAGERS AND YOUNG ADULTS WITH SARCOMA – BLACK SHEEP OR JUST PART OF THE CROWD?

J.S.Whelan
London Sarcoma Service, University College Hospital, London NW1 2PG

Sarcomas account for 10% of cancers occurring in 15-24 year olds. Within this group there is considerable clinical and biological heterogeneity and incomplete understanding of optimal treatments.

Most clinical research attention has focused on the management of bone sarcomas, particularly osteosarcoma and Ewing's tumours. Several factors have been studied which consistently identify patient groups with differing outcomes. Age at diagnosis appears to affect prognosis in Ewing's tumours but less obviously in localised extremity osteosarcoma. Any underlying biological or treatment delivery variables which may explain these observations have yet to be elucidated. Whether different treatment approaches for bone sarcomas should be adopted for teenagers and young adults (TYA) is unclear and will require systematic prospective evaluation.

Soft tissue sarcomas affect all ages. The numerous histiotypes are not evenly distributed across all age ranges. In the progression from childhood through adolescence to adulthood, rhabdomyosarcoma is replaced as the commonest subtype by the many different subtypes recognised by adult oncologists. There is little guidance about appropriate management of 'adult-type' soft tissue sarcomas occurring in TYA and this group have not been systematically studied. Their representation within clinical trials may be biased towards those with adverse features. There is considerable variation in practice particularly regarding the use of adjuvant chemotherapy. Few studies address whether specific approaches to treatment are appropriate for TYA with soft tissue sarcoma.

In the future, biologists and clinicians familiar with sarcomas affecting TYA and adults need to work together to share understanding and to design rational treatment programmes aimed at improving outcomes for TYA.

1.O.02

COMPARING ADULT AND PEDIATRIC RHABDOMYOSARCOMA IN THE SURVEILLANCE, EPIDEMIOLOGY AND END RESULTS PROGRAM, 1973-2005: AN ANALYSIS OF 2600 CASES

I.Sultan, I.Qaddoumi, S.Yaser, C.Rodriguez-Galindo, C. Meazza, M.Casanova, A.Ferrari
Pediatric Oncology Unit, Istituto Nazionale Tumori of Milan

Rhabdomyosarcoma (RMS) is one of the typical tumors of childhood and adolescence, but it is exceedingly rare in adults. Unfortunately, the treatment success achieved over the years for pediatric RMS has not translated into better cure rates for adults, who continue to have a very poor prognosis (overall survival rates of only 20-40%). To better characterize adult RMS, we performed an analysis of all RMS cases registered on the Surveillance Epidemiology and End Results (SEER) public-access database collected from various geographic areas in the United States from 1973 to 2005.
We analyzed 2600 patients, 1071 adults (>19 years) and 1529 children (≤19 years). Tumors in adults were more likely to be at an unfavorable site (65% *vs.* 55%; $P<0.0001$) and to have histologies that are unusual during childhood, particularly the pleomorphic subtype (19%) and not otherwise specified (43%). Regional and distant spread was not significantly higher in adults. Adults had significantly worse outcome than children (5-year overall survival 26.6% and 60.5%, respectively; $P<0.0001$). Adults had significantly worse outcome also analyzing subset of patients with similar tumors (i.e. same histotype, same stage). The most significant difference was in localized disease; 5-year overall survival rates were 82.2% and 46.8%, respectively ($P < .0001$). Multivariate analysis showed that age, histologic subtype, primary site location, stage, treatment with surgery, and treatment with radiation were significant predictors of survival. However, alveolar subtype and unfavorable primary site lost significance when analysis was restricted to adults.
In conclusion, our analysis confirmed that adult RMS was associated with a very poor outcome, especially in contrast to the significant improvements achieved in children treated contemporarily. The outcome for adults is consistently worse regardless of clinical characteristics, suggesting that factors other than an unfavorable clinical presentation might be involved in their unsatisfactory treatment results.

1.O.03

TNM STAGING IN EWING SARCOMAS: A MODEL FROM THE (EI)CESS/EE99 STUDIES

H. Juergens, D. Manner, J. Gerss, A. Ranft, M. Paulussen and U. Dirksen
University Hospital Muenster, Germany, Dept. of Pediatric Hematology and Oncology, Dept. of Medical Informatics and Biomathematics

Tumor size and metastases are known risk factors in Ewing tumors. Adequate staging is essential to stratify treatment intensity, but TNM staging is not established.
The validity of TNM staging was tested based on tumor volume (T1 ≤200 ml; T2 >200ml ≤500 ml; T3, >500 ml), the presence or absence of lymph node metastases (N0, N1), and distant metastases (M0, no metastases; M1 lung/pleura metastases; M1a ≤5 nodules; M1b >5 lesions; M2 bone metastases; M2a, 1 lesion; M2b >1 lesion and/or microscopic bone marrow contamination; M3, multi-system metastases). 1799 Ewing sarcoma patients of the (EI)CESS/EE99 studies entered into the Muenster database from 1981-2008 were analyzed.
Ten-year event-free survival (EFS) was 0.46. EFS in patients without metastases (T1-3N0M0) was 0.56 compared to 0.22 in metastatic patients (T1-3N0,1M1-3), p<.0001. In non-metastatic patients, tumor volume discriminated EFS: T1:0.62; T2:0.43; T3:0.40, p<.0001. The rare event of lymph node metastases correlated with unfavorable prognosis (N0:0.47, N1:0.12, p<.0001). The difference in EFS between pulmonary, skeletal and multi-system dissemination was significant: M1:0.29, M2:0.23; M3:0.12, p<.0001. The discrimination of M1 subgroups (M1a/M1b) was of prognostic relevance (p=.0050); M2 subgroups (M2a/M2b) discriminated outcome less clearly (p=.0457).
TNM staging is appropriate in Ewing tumors and should be incorporated in future trials.

1.O.04

AN UPFRONT SCORE FOR PRIMARY DISSEMINATED MULTIFOCAL EWING TUMOR PATIENTS PREDICTING OUTCOME - RESULTS FROM THE EURO-E.W.I.N.G. 99 TRIAL

R. Ladenstein, U. Pötschger, M.C. Delay, J. Whelan, M. Paulussen, O. Oberlin, A. Craft and H. Jürgens for the EuroEwing 99 Trial Group.
St. Anna Children's Hospital and Children's Cancer Research Institute, Vienna, Austria

The Euro-E.W.I.N.G. 99 trial aimed to improve the dismal prognosis of patients with primary disseminated multifocal Ewing tumors (PDM-ET) with a dose-intense treatment concept.
From 1999 to 2005, 281 patients with PDM-ET were enrolled onto the EURO-E.W.I.N.G. 99 trial. Median age was 16.2 years (0.4-49). Recommended treatment consisted of 6 VIDE, one VAI cycle, local treatment (surgery and/or radiotherapy), and high-dose busulfan-melphalan followed by autologuous stem cell transplantation (HDT/SCT).
After a median follow up of 3.8 years, event-free survival (EFS) and overall survival (OS) at 3 years for all 281 patients were 27%±3% and 34%±4%. Six VIDE cycles were completed by 250 patients (89%); 169 (60%) received HDT/SCT. Forty-six children less than 14 years and HDT/SCT achieved a 3-year EFS of 45%. Cox regression analyses demonstrated increased risk at diagnosis for patients over 14 years (HR 1.6), a primary tumor volume >200ml (HR 1.8), more than one bone metastatic site (hazard ratio: HR 2.0, bone marrow metastases (HR 1.6) and additional lung metastases (HR 1.5). An "up front" risk score based on these HR factors identified three groups with EFS rates of 50% for score ≤3 (82 patients), 25% for score >3 to <5 (102 patients), and 10% for score ≥5 (70 patients), p< 0.0001.
PDM-ET patients may survive with intensive multimodal therapy. Age, tumor volume, and extent of metastatic spread are relevant risk factors. A score based on these factors identifies PDM-ET patients may facilitate risk adapted treatment approaches.

1.O.05

ONCOLOGICAL OUTCOMES OF PATIENTS WITH EWING'S SARCOMA - IS THERE A DIFFERENCE BETWEEN BONY AND SOFT TISSUE EWING'S SARCOMA?

A. Pradhan, R. J. Grimer, A. Abudu, R. M. Tillman, S. R. Carter and L. Jeys
Royal Orthopaedic Hospital Oncology Service, Birmingham B31 2AP, UK

Ewing's sarcoma principally arises in bone but can also present as a soft tissue tumour. Very few studies have assessed the outcomes of extra-skeletal Ewing's sarcomas. This study compares the oncological outcomes of the two forms of Ewing's sarcomas to see if there is any difference in prognostic factors.
198 patients with primary, non metastatic Ewing's sarcoma diagnosed between 1980 and 2005 were identified from our database. There were 118 males and 80 females with a median age of 15 years. The three most common sites of diagnosis were the femur (24%), pelvis (15%) and tibia (13%). There were 169(85%) bony Ewing's and 29 (15%) extra-skeletal Ewing's sarcomas. All patients received chemotherapy. 86% of the patients had surgery for local control but 28(14%) patients had radiotherapy.
The overall survival at five years was 89% and was related to the age of patient (92% < 16years $p=0.005$), size ($p=0.03$) and site of tumour ($p=0.004$) as well as the response to chemotherapy. There was no difference in the overall survival of patients with bony Ewing's (90%) and extra-skeletal Ewing's (85%) ($p=0.85$). There was a 10% risk of local recurrence at 5 years with site of tumour ($p=0.01$) and surgical excision ($p=0.05$) being significant prognostic factors. The risk of local recurrence was also not related to the type of Ewing's sarcoma.
This large series has shown that the oncological outcomes of Ewing's sarcoma is related to tumour characteristics, patient age and treatment factors and not determined by the tissue component.

1.O.06

IS INSTITUTION A PROGNOSTIC FACTOR IN ADOLESCENT AND YOUNG ADULT PATIENTS WITH OSTEOSARCOMA?

D. Carrle[1], B. Blank[1], M. Paulussen[2], P. Reichardt[3]. S. Bielack[1,4]
[1]COSS Studienzentrale, Klinikum Stuttgart - Olgahospital, Zentrum für Kinder- und Jugendmedizin, Pädiatrie 5 (Onkologie, Hämatologie, Immunologie), Bismarckstr. 8, D-71404 Stuttgart
[2]Universitätskinderspital beider Basel, Onkologie/Hämatologie, Basel; Ch
[3]HELIOS-Klinikum Bad Saarow Sarkomzentrum Berlin-Brandenburg, D
[4]Universitätsklinikum Münster, Klinik und Poliklinik für Kinder- und Jugendmedizin, Pädiatrische Hämatologie und Onkologie, Münster, D

Purpose: Compared to paediatric cancer patients adolescents and young adults may have disadvantaged access to care. Therefore we investigated the correlation of patient, tumour and institutional characteristics with the outcome of osteosarcoma in this age group.
Method: Analysis of consecutive patients aged 15-24 years with newly diagnosed high-grade osteosarcoma entered into the Cooperative Osteosarcoma Study Group(COSS) registry 1980-2004 and treated in pediatric (PO) or medical oncology institutions (MO). Standardised multimodal therapy according to a COSS-protocol. Event-free survival rates (EFS) evaluated in relation to patient demographics and registering institution (MO vs PO and treatment volume as: <1, 1-3 or >3 osteosarcoma/year).
Results: 944 patients identified (median age: 17.35 years; range: 15.01-24.99; 79% aged < 20 years). Patients $\geq$ 20 years were more likely than younger patients to be treated in centers with low treatment volume ($p<.0001$) and MO ($p<.0001$) but otherwise comparable. After a median follow-up of 5.59 years (range: 0.12 - 27.92) for all patients and 8.08 years (range: 0.19 - 27.92) for 617 survivors, actuarial 5/10 year event-free survival probability (EFS) was 58%/54%. Upon univariate analysis of the total cohort neither of the institutional variables correlated significantly with EFS. There was a correlation between treatment in PO and improved EFS for patients $\geq$ 20 years ($p=.001$) and for those with primary metastases ($p=.009$). Upon multivariate testing type of center (odds ratio: 1.26; $p=.022$) but not treatment volume were significant.
Conclusion: Within a framework of standardised regimens and consultation support by our group's infrastructure, similar EFS-probabilites were obtained regardless of institutional treatment volumes. Observed variations in outcome between PO and MO may be partly due to different distributions of presenting factors but deserve further investigation.
Acknowledgement:
Supported by Deutsche Krebshilfe, Thanks to M. Kevric and E. Hallmen for data management.

1.O.07

ANEURYSMAL BONE CYSTS – SIMPLE TREATMENT WORKS!

F. Sinnaeve, R.J. Grimer, S.R. Carter, R.M. Tillman, A. Abudu, L. Jeys
The Royal Orthopaedic Hospital Oncology Service, Birmingham B31 2AP, UK

Aim: To review our experience of managing patients with aneurysmal bone cysts (ABCs).
Method: We reviewed the medical records and radiographs of all patients with ABCs treated at our unit over a 25 year period. During that time the policy of the unit was to treat ABCs with biopsy/curettage without use of adjuvants or bone grafting. Patients were followed up with regular Xrays until healing had taken place. Local recurrences were again treated with curettage, occasionally supplemented with embolisation or bone grafting.
Results: 237 patients (128 female, 109 male), with a median age of 14 yrs (range 1 to 76), received treatment. The cyst size varied from 1 to 20 cm and the median duration of symptoms was 16 weeks (range 0 to 8 yrs). The most common sites were the tibia (55), followed by the femur (41), then the pelvis (29) and the humerus (27). Thirty-five (15%) of the patients presented with a pathological fracture.
Primary treatment was by curettage alone in 195, curettage and bone grafting in 7, aspiration and injection of steroids or bone marrow in 7, excision in 5 and observation alone in 17. The rate of local recurrence requiring further surgery was 12% with all local recurrences (but one) arising within 18 months. Local recurrence was not related to site, age, sex or whether the patient had previous treatment or not. Local recurrences were managed with curettage alone in 19 of the 23 cases, with one having embolisation, one excision and 2 curettage and bone grafting. This was successful in all but 3 cases who were controlled with a third procedure.
Conclusion: The local control rate of ABCs with simple curettage is 88%, which is as good as the results published for any other technique. We recommend biopsy in all cases with limited curettage at the same time, and many ABCs will heal with this simple procedure. Full curettage is needed for those showing no signs of healing within 4 weeks. Local recurrence is very unusual after 18 months.

1.O.08

CURRENT CONCEPTS ON THE MOLECULAR BIOLOGY OF OSTEOSARCOMA

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Osteosarcoma despite considerable biological and molecular heterogeneity, being defined by a phenotypic program resulting in the production of osteoid, is a relatively consistent clinical entity. Over the past 20 years a large catalogue of genetic alterations present in osteosarcoma has been compiled, but unfortunately this information has yielded little biological understanding or widely accepted prognostic factor. In an analogous manner nearly two decades of clinical trials, most incorporating new agents or intensifying therapy have not further improved the prognosis of patients with osteosarcoma. This would lead to considerable pessimism if it were not for the dramatic expansion in availability of osteosarcoma models, tissues resources as well as new agents, particularly antibodies targeted to various cell surface receptor proteins. Selecting and applying these agents will require an understanding of osteosarcoma's unique dependencies and may also have the potential to yield biological insights. Defining these dependencies has been complicated by osteosarcoma's genetic complexity as well as redundant expression of cell surface receptors, but efficacy of antibody-based targeted therapies may assist in defining the relative importance of receptors as well as their downstream signal transduction pathways. The availability of these new tissue resources and murine models may assist in understanding osteosarcoma's complex biology, aid identification of biological features that can serve as prognostic factors as well as assist in the selection of new agents for clinical trials. These new resources may permit one to define the feasibility of performing a biologically based treatment selection and may have implications for cooperative group interaction. During this presentation the molecular biology of osteosarcoma will be reviewed, the available tissue resources and models will be outlined, some of the preliminary data available thus far will be presented, and this will be placed in the context of ongoing as well as planned phase 1 and phase 2 osteosarcoma clinical trials.

1.P.01

SYNOVIAL SARCOMA OF THE FOOT

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Synovial Sarcoma of the foot is the most common soft tissue sarcoma to present in the foot. Despite this, diagnosis is often delayed and treatment may be difficult. The aim of this paper is to review the presenting features, management and outcome of synovial sarcoma of the foot and to try and identify areas for improvement.
33 patients with synovial sarcoma were treated at out unit over a 25 year period. The average duration of symptoms was 125 weeks. The age range at presentation was 11 to 80 years (mean 44). The mean size of the tumour at diagnosis was 5cm in diameter (range 1-10cm). 75% of the tumours were deep at the time of diagnosis. Treatment was by amputation in 21 patients and limb salvage in 11 with 1 patient receiving palliative chemotherapy. Only one patient had local recurrence and presented with lung metastases. Four patients had metastases at diagnosis and nine developed them subsequently. Overall survival at 10 years was 53%.
These results have shown that late diagnosis is common for synovial sarcoma of the foot and that by the time of diagnosis 75 % have invaded extra-compartmentally leading to a high risk for amputation. 20 patients had an inadvertent excision of the tumour before referral to our unit. Local control was best achieved with amputation. Overall survival was surprisingly poor despite successful local control. Earlier aggressive investigation of patients with foot pain or swelling but no other features may change their long term prognosis.

1.P.02

EXTRACORPOREAL IRRADIATION FOR PELVIC RECONSTRUCTION IN EWINGS SARCOMA

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This study reviews the implantation of extracorporally irradiated autografts as a treatment modality and alternative for pelvic Ewing's Sarcoma.
We identified 13 cases between 1994 and 2004 (7 male, 6 female), with mean age 14 years (6.5-34.5). The disease free survival was 69% overall, (75% excluding one case initially treated elsewhere) with a mean follow-up of 6.1 years (3.1 - 8.2). Four patients died with distant metastases at a mean time of 17 months (13-23).
Functional results showed a median MST-Score of 86% (IQR 68.5 to 91.5), a median TES-Score 85% (IQR78.5 to 93.5) and a median Harris Hip-Score 89 % (IQR 82.5 to 96.5).
Solid bony union was observed at all osteotomy sites. Consolidation was achieved after median 6 months (IQR 5 to 7).
There were three complications (23%) which required operative intervention, one (8%) due to infection, which required removal of the autograft.
Advantages with this technique include ideal fit in the defect and thus promotes healing through greater contact at osteotomy junctions. It avoids early and late loosening and/or breakage of a prosthesis. It acts as a biological bridge for creeping substitution and bony incorporation in the defect. It allows re-attachment of tendons and ligaments, and thus preserves anatomic relationships. There is no risk of disease transmission or immunological reactions. It is cost effective and convenient in any institution with radiotherapeutic equipment.
We conclude this is an appropriate treatment option for localised and resectable pelvic Ewing Sarcoma.

1.P.03

TREATMENT OF LOCALIZED EWING'S FAMILY TUMORS OF THE RIBS IN CHILDHOOD WITH INTENSIVE MULTIMODAL THERAPY: SINGLE CENTER EXPIRIENCE

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We analyzed the results of the intensive multimodality therapy of children with localized Ewing's family tumors of the ribs (EFTR). 22 patients with localized EFTR were treated in our institute between 1996 and 2006. The age is ranged from 4 to 15 years. 10 patients were male, 12 — female. Eight patients had a classic Ewing sarcoma(ES), 14 —PNET. The high risk criterion was tumor volume over 100 ml. The treatment plan included intensive induction chemotherapy (adapted to risk group) consist of 5 courses (1, 3, 5 courses — vincristine, adriamicin, cyclophosphamide, 2, 4 courses — ifosfamide and etoposide) and local control (surgery and radiotherapy), and consolidation with or 5 courses standard therapy or high-dose chemotherapy with stem-cell rescue. 4 patients underwent high-dose chemotherapy, 18 — consolidation with standard arm.
Two patients died from complications of chemotherapy, 20 patients completed the treatment. 5-year overall survival (OAL) of patients was 70±10,4%, 5-year event-free survival (EFS) was 58,9±11,4%. We conclude that Ewing's family tumors are the most common tumors of ribs in childhood. Improved EFS requires more aggressive systemic chemotherapy and surgery (removing of entire affected ribs). Long-term survival is possible, even for high risk patients.

1.P.04

MODERATE WEIGHT LOSS UNDER EWING SARCOMA TREATMENT DOES NOT IMPAIR OUTCOME IN PATIENTS FROM THE (EI)CESS TRIALS.

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Background: Intensive chemotherapy in sarcoma treatment may lead to weight loss, and in turn reduce dose intensity. A possible correlation between weight loss under treatment and outcome has never been analysed in sarcoma treatment. Ewing sarcoma (ES) patients undergoing intensive non-corticosteroid-containing chemotherapy commonly experience weight loss. The German Paediatric Oncology/Haematology Society (GPOH) Ewing sarcoma trials (CESS, EICESS) registry was analysed with respect to weight loss and outcome.
Patients and Methods: Body weight (BW) both at diagnosis and after a median of 12 courses of chemotherapy was available in 837 of 1549 ES patients, excluding amputees. Changes in BW were calculated as percentage of initial BW; outcome was determined as event-free-survival (EFS) from diagnosis according to Kaplan-Meier. Correlations of BW and outcome and potential confounders like disease stage or tumour volume were estimated uni- and multivariately.
Results: Weight loss was not correlated with inferior outcome: A loss of 10%-20% of BW was associated with a slightly more favourable outcome (3-year EFS 0.64 +/-0.106, N=82) than weight gain of 10%-20% of BW (3-year EFS 0.58 +/-0.098, N=97), p=0.101. Multivariate analyses revealed no confounders interfering with these results.
Conclusions: In 837 ES-patients analysed, weight loss did not correlate with inferior outcome. This should be observed in discussions about tube feeding and/or parenteral nutrition under cytostatic therapy. Future analyses of the prognostic impact of extreme under- or overweight both at diagnosis or under treatment are warranted in order to develop appropriate guidelines. Validity of this observation should be analysed for other solid tumours.

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1.P.05

EWING'S SARCOMA OF THE VERTEBRAE- RESULTS OF A SINGLE INSTITUTE FROM SERBIA

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Purpose: Treatment results in patients with Ewing tumors of the vertebrae were analyzed.
Patients and Methods: Between June 2000 and April 2007 7 patients with primary tumors of the thoracic or lumbar vertebrae were treated. No one patient had primary tumor of the cervical vertebra. The median ageat diagnosis was 13 years (range, 12 to 18 yrs.). Primary sites: thoracic5, lumbar 2. No one had metastases at diagnosis. Surgery was performed in 5 pts. Complete surgical excision in 2 and maximal tumor reduction in 3.Only biopsy was in 2pts. After surgery all pts. received chemotherapy: EICESS 92 (EVAIA chemotherapy regimen) in 4 pts. and Euro Ewing 99 in 3 pts. Radiotherapy was performed in 6 patients: after 2 cycles of chemotherapy in 2 pts., after 3 cycles in 4 pts. Median dose 5040cGy (range 5018-5400cGy) in conventional fractionation. Daily fractionation from 180-193cGy.
Results/ Discussion: The mean follow-up was 41 months (range 4-104 months). Overall survival (OS) rate was 71,42 %. One patient progressed and died after complete treatment, another one died during chemotherapy before radiotherapy. In our series of Ewing's Sarcoma of the vertebrae, good surgery initialy, early definitve radiotherapy and aggressive multimodal therapy (surgery/radiotherapy/chemotherapy) may be effective in disease control and survival.

1.P.06

CHEMOTHERAPY REGIMENS IN OSTEOSARCOMA RELAPSE

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Objective: The aim of our study was to evaluate results of chemotherapy regimens and analyse prognostics factors in children with relapse of osteosarcoma.
Patients and methods: From 2000-2007, we treated 57 patients with non metastatic osteosarcoma, median age 15,5 years (range 3-18). 29 pts relapsed. 26 pts with osteosarcoma relapse were treated, and 3 pts with OS relapse refused the treatment. In 24 pts pulmonary metastases were detected (7 solitary), while 2 pts had local relapse of disease. Disease free interval (DFI) was more than 1 year in 12 patients. Surgery was performed in 20 pts (17 thoracotomy, 3 amputation). Chemotherapy regimens administered were: HD IFO-VP16 (11 pts), HDMth / IFO-VP16 (6 pts), HDMth/ Carbo-VP16 (9 pts).
Results : During 8-116 months follow up period (Me=32 mts), disease free suvival rate was 33.12%. There was no significant difference in survival in relation to the type of chemotherapy regimen applied.Prognostic factors that influenced survival were: presence of a solitary metastasis (p= 0.026), local relapse of disease (p= 0.002), completeness of resection (p=0.043) and DFI longer than 1 year (p= 0.039).
Conclusion: The use of aggressive multimodal therapy (surgery/chemotherapy) and evaluation of prognostic factors are necessary for successful treatment in patients with osteosarcoma relapse. Chemotherapy regimen HD IFO-VP16 had better initial tumore response, but in longer follow up the survival rate was similar to other chemotherapy groups.

1.P.07

OSTEOSARCOMA IN RETINOBLASTOMA SURVIVORS: MOLECULAR ANALYSIS AND RESULTS OF MULTIMODAL MANAGEMENT

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Osteosarcoma is the most common second malignancy seen in retinoblastoma survivors. Risk of developing osteosarcoma in this group is estimated approximately 500 times higher than the general population. Prognosis in this setting has been reported significantly worse than conventional osteosarcoma despite multimodal management. Purpose of this study was to evaluate clinical features, molecular aspects and outcome of treatment in this subgroup of osteosarcoma patients.
Between 1985 and 2004, from a total of about 1100 osteosarcomas, 7 survivors of retinoblastoma developing high-grade osteosarcoma as second malignancy presented at the authors' Institution. Retrospective study was undertaken to analyze presentation, tissue expression of RB1, P53, PGP and DHFR, treatment and outcome of both retinoblastoma and osteosarcoma.
Retinoblastoma was bilateral in 5 cases and unilateral in two. All the patients had been treated with a combination of surgery +/- chemotherapy +/- radiation.
None of them had evidence of retinoblastoma at the time of second malignancy diagnosis. Average age at diagnosis of osteosarcoma was 14 years (9-17 years), mean interval between the two malignancies was 155 months. All the osteosarcomas were in the appendicular skeleton, all but one around the knee. Molecular analysis showed defective RB1 gene in all cases All the seven patients received contemporary multimodal management for osteosarcoma. All but one patient died of osteosarcoma within 30 months from diagnosis. The living patient had local recurrence 9 years after limb salvage and is currently disease free following amputation.
Prognosis of osteosarcoma in retinoblastoma patients remains poor as compared to conventional high grade osteosarcoma despite multimodal management. No obvious correlation was found between poor prognosis and P53, PGP and DHFR expression.

1.P.08

IFOSFAMIDE-CARBOBLATIN CONTAINING CHEMOTHERAPY IN REFRACTORY/ RECURRENT OSTEOSARCOMA AND MALIGNANT FIBROUS HYSTIOCYTOMA (MFH)

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The purpose of study was to evaluate retrospectively the efficacy of Ifosfamide-Carboplatin containing chemotherapy in recurrent/refractory osteosarcoma and MFH of the extremities. Twenty seven osteosarcoma and 2 MFH pts who had achieved complete surgical remission after multimodal treatment and then progressed soon after en-bloc bone resection or developed recurrent disease were included in two chemotherapy protocols. There were 20M/ 9F with ages ranging from 15 to 36 yrs (mean 20). Chemotherapy consisted of ifosfamide (median dose per cycle 7.5 g/m^2) + carboplatin (median dose 350 mg/m^2) + etoposide (median dose 450 mg/m^2) - (regimen ICE) or doxorubicin 60 mg/m^2 (regimen ICA). Response was evaluated according to RECIST. Survival was calculated from the time of R1 to death and analyzed as February 11, 2009. In total 93 (from 1 to 5. mean 3) cycles were administrated between October 2003 and December 2008. Of 17 ICE pts 3 had PR (17.6%), 10 had SD (58.8%) and 4 (23.5%) – PD. Among 12 ICA pts 3 (25%) had PR, 6 (50%) had SD and 3 (25%) had PD. Sixteen pts (55%) without progression during chemotherapy achieved second surgical remission. At last follow-up 12 pts died of disease, 8 are AWD and 9 are NED. Actuarial 5-year survival was 35±16%, median 38 mos. Outcome was related to relapse-free interval. Five-year survival was 23±18% among patients who relapsed <12 mos after CR1 and 64±18% among pts who relapsed later, p=0.3. 5-year survival was significantly better in pts in whom chemotherapy was followed by surgery for distant metastases - 37.8±27% (median 38 mos), versus 23.3±19% (median 11 mos.) in patients treated without surgery, p<0.05.
We conclude that retrieval chemotherapy stopped disease progression in the majority of cases. Followed by surgery it was associated with better survival. These regimens and treatment strategy need further investigation in prospective trials.

1.P.09

ONCOLOGICAL OUTCOME FOLLOWING LIMB SALVAGE SURGERY DONE FOR HIGH GRADE OSTEOSARCOMA PATIENTS WHO WERE INITIALLY TREATED INADEQUATELY BY CURETTAGE OR DRAINAGE

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Patients with high-grade osteosarcoma who have been previously misdiagnosed as benign lesions or infection and accordingly been treated by curettage, internal fixation or drainage present a challenge in deciding the most appropriate treatment plan. Since one of the contraindications of limb salvage is the inability to achieve a wide surgical margin, there has been a tendency to treat these patients by amputation. Due to contamination by previous surgeries, limb salvage surgery was thought to be associated with a higher risk of local recurrence.
The aim of this study was to evaluate the oncologic outcome following limb salvage surgery done for high-grade osteosarcoma patients who were initially treated inadequately by curettage, internal fixation or drainage.
The study included 24 patients (14 males and 10 females) with an average age of 19 years (range 7 to 39 years). All the patients had high-grade osteosarcoma of the extremities. Seven were located in proximal tibia, six distal femur, four proximal humerus, three proximal femur, two distal tibia, one distal radius and one fibula. 14 patients were previously diagnosed as benign lesions and treated by curettage. 5 patients were diagnosed as regular fracture and internally fixed. 5 patients were diagnosed as osteomyelitis and treated by drainage. The patients were staged then treated by neoadjuvant chemotherapy and limb salvage surgery. The average time between the initial procedure and the limb salvage procedure was 7 months (range 3 to 36 months). A wide resection margin was achieved in all patients.
The average follow up period was 40 months (range 18 to 110 months). Local recurrence occurred in three patients (12.5%). Three patients developed chest metastases and one patient developed bone metastases.
We conclude that patients who had an inadequate surgical procedure prior to the diagnosis of a high-grade osteosarcoma could still be treated by neoadjuvant chemotherapy and limb salvage surgery without a significant increased risk of local recurrence and chest metastases.

1.P.10

FUNCTIONAL AND ONCOLOGIC OUTCOME OF OSTEOSARCOMA IN CHILDREN AND ADOLESCENTS: A RETROSPECTIVE STUDY OF 120 CASES (EXPERIENCE OF CAIRO UNIVERSITY HOSPITALS)

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Osteosarcoma is the most common bone tumour of the paediatric age. Long time survival can be reached in 70% of patients when metastatic disease is absent at presentation. But in spite of aggressive chemotherapy regimens, about 30% of patients die of the disease.
This retrospective study was carried on 120 patients with primary non-metastatic osteosarcoma of the extremities, attending at Cairo University Hospitals (Faculty of Medicine and National Cancer Institute) between January 1993 and June 2006. The patients' functional outcome was evaluated according to the Musculoskeletal Tumor Society Functional Rating System.
All patients have undergone surgical resection of the tumour and limb salvage. They have received different chemotherapy regimens depending on the time of entry to the study. Four patients were treated according the Osteosarcoma Group Study I (OSGI): six courses of adjuvant cisplatin and doxorubicin. Twenty patients received OSGII: 2 neo-adjuvant and 4 adjuvant courses of cisplatin and doxorubicin. Twenty-nine patients received OSGIII: high-dose methotrexate, ifosfamide, doxorubicin, and cisplatin. Sixty-seven patients received OSGIV: high dose cisplatin, ifosfamide, doxorubicin and a cardioprotective agent. Patients with limb salvage surgery were divided into 3 groups: mobile joints (33 patients), fused joints (75 patients) and rotation plasty (12 patients).
The 5-year event free survival and overall survival for the 120 patients were 70.9 % and 71.3% respectively at median follow-up of 54.5 months and a range of 5-153 months. Functional outcome for available patients according to MST rating system was $<70\%$ in 34 patients and >70 % in 86 patients. There was not a statistically significant difference between survival and different prognostic factors (age, sex, tumour site, tumour size, tumour necrosis, pathology and time of chemotherapy). Only serum LDH and alkaline phosphatase were statistically significant when correlated with survival.
The results of this study seem to be in accordance with other studies in the literature.

1.P.11

HOW TO STRATIFY PATIENTS WITH OSTEOSARCOMA. CLASSIFICATION AND REGRESSION TREE ANALYSIS

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In osteosarcoma, treatment guidelines recommend standard chemotherapy regardless of severity of disease. Treatment individualization will minimize risk of failure and adverse effects, specially in patients who have good prognosis. Therefore, there is a pressing clinical need to develop a risk adapted strategies and to adjust chemotherapy to prognostic factors.
Aim: to asses usefulness of Classification and Regression Tree Analysis (C&RT) for stratifying patients with localised osteosarcoma to the risk groups according to clinical and biological markers.
Material and methods: 100 patients with localised osteosarcoma were included, aged 5-23 years (mean 14), with extremity localisation of the primary tumour. Follow up – at least 5 years since a date of diagnosis. We analysed clinical prognostic factors (tumour size, pathological fracture, alkaline phosphatase, age), histological prognostic factors (% of viable tumour cells after preoperative chemotherapy, subtype of osteosarcoma and its aggressiveness) and biological factors (expression of VEGF, Ki-67, Topoisomerase II alpha and P glycoprotein). The expressions of proteins were measured immunohistochemically in biopsy samples. C&RT model included all described above factors.
Results: C&RT analysis revealed that the most important prognostic factors in localised osteosarcoma were: VEGF, Topoisomerase II alpha and tumour size. This markers were included into the risk classification and three risk groups were proposed: with poor prognosis (n=13) – 5 year OS 31%, moderate (n=57) – 5 year OS 63% and with good prognosis (n=30) – 5 year OS 93%), P=0.000.
Conclusion: C&RT is useful method for stratifying patients with osteosarcoma to risk groups. The stratification should include biological and clinical prognostic m

1.P.12

MODERN ASPECTS OF TREATMENT OF OSTEOSARCOMA

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Purpose of this study was to share our experience with combined therapy of patients with osteosarcoma of long tubular bones.
We have analyzed 173 patients with osteosarcoma-99 males and 74 females. The mean age was 18,5 years. Anatomical location included: femur-89 (51,4%) pts, tibia-41 (23,7%) pts, humerus-35 (20,2%) pts, other long tubular bones-8 (4,7%) pts. The following surgical procedures were performed: prosthetic reconstruction of the knee joint-71 (41,1%) pts, prosthetic reconstruction of the shoulder joint-14 (8,1%) pts, interscapular-thoracic resection-16 (9,2%) pts, segmental resection of bones with applying of Ilizarov's device-4 (2,3%), amputations and exarticulations-68 (39,5%) pts.
In all patients we have carried out combined therapy. In case of lower extremity tumour localisation at the first stage we have performed intra-arterial preoperative chemotherapy of DOX 90 mg/m2 as 72-hour, at the second stage surgery. The histological response was evaluated according to Huvos score. Adjuvant chemotherapy in good responders (grade III-IV) comprised the drugs used preoperatively, in poor histological responders (grade I-II) CAP scheme. In some patients ifosfamide and etoposide were added. In case of upper extremity tumour localisation induction chemotherapy consisted of 3 cycles of CAP scheme, surgical treatment and adjuvant chemotherapy with CAP scheme (3 courses) in good responders. In poor histological responders we have added ifosfamide and etoposide.
At localised forms of osteosarcoma 5-years survival rate was 52,1±1,4%. Functional results are good in most patients. Without extra support move about 80% patients. At local-spread forms survival at 5-years is worse- 48,1±1,2%.
In patients with metastatic disease we have not observed full remission. Achieved results testify that combined therapy (surgery and chemotherapy) is optimum at treatment of patients with osteosarcoma at present day and permits to attain full recovery and to improve life quality of patients.

1.P.13

THE PROGNOSTIC ROLE OF THE EXTRACELLULAR DOMAIN OF HER-2 AND ITS USEFULNESS FOR TREATMENT MONITORING IN OSTEOSARCOMA

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Serum level of the extracellular domain of HER-2 (ECD/HER2) has been suggested to be a tumor marker in breast cancer. The aim of this study was to assess the prognostic value of baseline level of ECD/HER2 and changes in levels over time in children and adults with osteosarcoma during chemotherapy.
Materials and methods: We analysed 33 newly-diagnosed osteosarcoma patients treated at the Department of Paediatric Oncological Surgery of the Institute of Mother and Child, Warsaw, Poland between 2005-2008. Patients characteristics: age 8-18 years (median 15); staging at diagnosis: disease localised (18) and dissemination (15); disease progression (13); deaths (6). Follow-up: 8-37 months (median 19). ECD/HER2 was measured in 118 serum samples using a validated ELISA kit: at the time of diagnosis (1), after preoperative chemotherapy (2), 2 weeks after surgery (3) and 3-6 moths after surgery (4).
Results: The baseline level of ECD/HER-2 in serum ranged 3.8-34.4 ng/mL (median 5). The elevated baseline ECD/HER2 was associated with decreased progression free survival (ECD/HER2 ng/mL>5 vs ECD/HER2 ng/mL≤5: 44% vs 77%; p=0.039) and decreased overall survival (ECD/HER2 ng/mL>5 vs ECD/HER2 ng/mL≤5: 69% vs 94%, p=0.115). The concentration of ECD/HER2>6 ng/ml during treatment (specially postoperative chemotherapy) was associated with early disease progression (p=0.095).
Conclusions: The high level of ECD/HER2 at the time of diagnosis may be a marker of poor prognosis in osteosarcoma. Additionally, we suggest that changes of this marker concentration over time could be helpful for treatment monitoring.

1.P.14

OSTEOSARCOMA IN PEDIATRIC AND YOUNG ADULTS PATIENTS IN SINGAPORE: A SOUTH EAST ASIAN EXPERIENCE

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We attempted to investigate the incidence, the treatment modalities used and the outcome of Osteosarcoma (OS) patients treated at the two major Pediatric Oncology Hospitals in Singapore. A comprehensive list of patients with OS treated at the National University Hospital and KK Women's and Children's Hospital Singapore between April 1980 and May 2006 was generated. During the study interval, patients received neoadjuvant chemotherapy followed by definitive surgery consisting of either limb salvage or amputation followed by adjuvant chemotherapy. Chemotherapy was as per the European Osteosarcoma Intergroup (EOI) and as per the Memorial Sloan-Kettering Cancer Center's (MSKCC) T12 protocols. Treatment of subsequent relapses consisted of various combinations of Methotrexate, ifosfamide, etoposide, other, and / or surgery. Of the total 49 patients with OS, 30% presented with metastatic OS. Median age of diagnosis of OS was 12.4 years. For the cohort, two and five-year overall survival were 71% and 55% respectively. The two-year overall survival was 73% for patients who were treated as per the MSKCC protocol. At last follow-up, median 4.3 years (range, 0.3 - 21.6 years), 25 were alive with no evidence of disease and 16 were dead of disease.
Survival from OS in Singapore appears to be improving. Rarity and complexity of OS makes it crucial for patients to seek a centralized multi-disciplinary Musculoskeletal Oncology team involving surgeons and Pediatric Oncologists dedicated to the care of these young patients with the intent to cure.

1.P.15

OSTEOSARCOMA TREATMENT WITH BISPHOSPHONATE PAMIDRONATE DISODIUM AS A MAINTENANCE THERAPY

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Osteosarcoma is the most frequent bone tumor in adolescents and young adults. Already, the bisphophonates were introduced as the first line therapy for metastatic disease as well as the maintenance therapy, but new drugs are still in researchers interest.
Between 2005 and 2008, we have been treated 17 osteosarcoma patients, from 4 till 18 years of age. All patients have been followed up for 11 months average (range 4-18). At the time of diagnosis 15 of them had local disease, and 2 had metastatic disease. They were treated according to EURAMOS protocol. There were two groups of patients; the high risk patients who has received the pamidronat disodium (pamidronat) after the standard postoperative chemotherapy, and the other group who hadn‘t received pamidronat. One patient, who had bone and pulmonary metastasis at the diagnosis, received the pamidronat as the first line therapy. We have introduced the 2 mg/kg mothly of pamidronat to 7 patients, median age of 13. Patients have received 8 cycles average of pamidronat (range 4-12). Two patients had to be excluded from therapy due to nephrotoxycity and pregnancy. The patient with metastatic disease, bone and lung metastasis, at the diagnosis, had died, and two patients who had pulmonary metastasis, afer the surgery and second line chemotherapy, showed no disease progression during the pamidronat therapy. In the other group of patients, who hadn‘t received the pamidronat, one patient with metastatic disease had died, 2 of them had local reccurence, and 2 died due to disease progession.
Introducing the pamidronat has been a big step forward for osteosarcoma patients, because, according to our results, during the pamidronat therapy they haven’t developed local recurrence and/or disease progression.

1.P.16

INTENSIVE CHEMOTHERAPY WITH HIGH DOSE METHOTREXATE AT THE OSTEOSARCOMA IN CHILDREN

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The aim of our study was to increase of survival of children with osteosarcoma by intensification of chemotherapy by inclusion of high dose methotrexate. 53 patients were treated in our centre between 2003 and 2007. Age are ranged from 5 to 16 years. 23 (43,4%) patients had metastetic disease. Polychemotherapy consist of alternating courses of CDDP, adriamicin, ifosfamide and etoposide and high-dose methotrexate (8-12 g/m²). In 25 (51%) cases have been received objective response (CR+PR). 38 (71,7%) patients alive at present time. 2 patients died from complications of treatment. 7 patients had PD, 1 — local relapse, 4 — metastatic relapse, 1 — combined relapse. 2-year OAS was 75,2±6,8%, 2-year RFS was 65±7,8%.

2.O.02

EUROBONET – OSTEOSARCOMA RESEARCH ACROSS THE BORDERS

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Networks of Excellence (NoE´s) are an instrument to overcome the fragmentation of the European research landscape with the objective to strengthen European excellence in a given area. Their purpose is to reach a durable restructuring/shaping and integration of efforts and institutions or parts of institutions in areas where this is necessary. The success of a NoE is not measured in terms of scientific results but by the extent to which the social fabric for researchers and research institutions in a given field has changed due to the project and the extent to which the existing capacities become more competitive as a result of this change. With that background a “European Network to promote research into uncommon cancers in adults and childrens: Pathology, Biology and Genetics of bone tumours” was initiated and founded by the European Commission in 2005 with the involvement of more than 20 institutions all over Europe.
Osteosarcoma research represents an own research line within this network. Up to now a multitude of experience has accumulated over the years which will be presented. The obvious advantages of a close cooperation between the network partners are a major hallmark and success of the network and should further lead to an improved translation of the basic research results towards a clinical application.

2.O.03

PROGNOSIS AND THERAPEUTIC TARGETS IN THE EWING FAMILY OF TUMOURS – 6TH FRAMEWORK PROGRAMME

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With modern polychemotherapy Ewing's sarcoma exhibit remarkable chemosensitivity leading to 5-year survival rates approaching 60-70%. However, in the last decade, no significant progress has been achieved in terms of improved cure rates and quality of life. In addition, prognosis is poor either in relapsed patients and in patients with metastasis at diagnosis. Thus, it is imperative to develop novel therapeutic strategies and to identify markers for risk-adapted therapies.

The PROTHETS European Consortium through collaborative studies defined prognostic markers and new therapeutic targets in the Ewing's sarcoma family of tumours (ESFT), to provide rigorous scientific justifications for the development of clinical trials for this rare disease. Genetic studies have been performed for the screening of high-risk patients and patients responding differently to chemotherapy.

Between others, these studies identified in gluthation metabolism a major pathway regulating Ewing's sarcoma chemoresistance. The prognostic relevance of glutathione metabolism pathway was validated by RT-PCR and the expression of MGST1, the microsomal glutathione transferase (GST), was found to clearly predict EWS prognosis. MGST1 expression was associated with doxorubicin chemo sensitivity. This prompted to assess the in vitro effectiveness a new anticancer agent (NBDHEX) that efficiently inhibits GST enzymes..

The consortium have collected more than 600 cases in specific tissue arrays for validation studies. Their use allowed the identification of some markers of prognosis, either conventional or new (ki-67, adhesion proteins, GAL3BP). Overall, theses studies started to define possible forthcoming risk-adapted strategies.

Another goal of the project was the creation of new tools and drugs as well as the optimization of molecular approaches against three therapeutic targets, EWS-FLI1, CD99 and IGF-IR that have great potential in terms of clinical application. The studies on IGF-IR have provide the rationale for the currently on-going clinical studies in Ewing's sarcoma.

2.O.04

CONTICANET :HARMONISING CONNECTIVE TISSUE CANCER RESEARCH AND TREATMENT DEVELOPMENT

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The CONnective TIssue CAncers NETwork to integrate European Experience in Adults and Children (CONTICANET) is dedicated to improve the outcome of connective tissue cancers in adults, adolescents and children. Funded by the European Commission's Sixth Framework Program (FP6-018806), this Network of Excellence kicked off in February 2006 for a five-year period. Ten work packages are grouped around the themes of "Integration" "Common research programme" and "Dissemination of excellence". A consortium of 24 different organisations – cancer centres, academic institutions, patient advocacy groups and private enterprises – hailing from 9 countries (Belgium, France, Germany, Ireland, Italy, the Netherlands, Spain, Slovenia, UK), including >250 researchers, is involved in collaborative research efforts that will help propagate excellence in the field. Improving the management of these tumours will come out the following outputs of the network activities:
- Epidemiology
- Molecular characterisation and nosological classification
- Understanding the deviations of medical practices and initiating corrective strategies
- Identifying new molecular targets and targeted treatments
- Promoting clinical research on very rare subtypes
- Addressing specific age (paediatrics, adolescents) or condition (Recklinghausen) group issues
- Organisation of the collection and storage of biological samples
- Standardisation of their management
- Identification of centres of excellence for pathological and biological management and clinical management, and the scientific promotion of shared and multidisciplinary research programs.

In addition, CONTICANET will integrate the expertise from other networks through collaborations, such as clinical research networks (EORTC, National sarcoma groups), other networks (EUROBONET, networks on rare tumors and paediatric/adolescent tumors). Afyer 5 years a legal entity will continue to spread excellence in several directions: enlarging the network with academic and private organisations; continuing to enhance relations with EMEA, health authorities, patients advocacy groups, cancer leagues. Together, we aim to a European research foundation able to support integrated research actions and make available new treatments in these diseases.

2.O.05

TRANSLATIONAL SARCOMA RESEARCH NETWORK (TranSaRNet)

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Sarcomas are rare malignant tumors of mesenchymal origin and primarily occur in children, adolescents and young adults. With multimodal treatment concepts survival has significantly improved and is now in the range of 60-70 %. Following relapse or metastasis, however, the prognosis still is poor as is also the case for patients presenting with primary disseminated disease. TranSaRNet aims to develop novel treatment strategies overcoming tumor cell resistance directed against novel targets. To achieve this goal the German pediatric, adolescent and adult sarcoma research groups have formed a collaborative network linking the nationwide and European trial groups with access to over 90 % of all pediatric and adolescent sarcoma patients and a large number of adult sarcoma patients to basic and translational sarcoma research groups. Within TranSaRNet a registry for patients at relapse is established as target cohort for innovative treatment strategies as well as a biomaterial banking network in order to facilitate the availability of tumor and other biomaterial for basic and translational research. A joint bioinformatics platform will integrate existing array data, to standardize laboratory and evaluation procedures and for modeling new theoretical concepts in a joint effort. Within the basic and translational research work packages, the sarcoma research groups in Germany have coordinated their research activities in a joint effort. The basic research work package (WP1) includes projects on genomic (WP1.1) and epigenetic (WP1.2) tumor characterization as well as identification of the tumor initiating cell (WP1.3) and resistance mechanisms (WP1.3 und 1.4), and the identification of new targets in apoptotic pathways (WP1.4, 2.4) and tumor-induced angiogenesis (WP1.5). The translational research work package (WP2) is focused on innovative immunological treatment strategies including sarcoma specific T-cells (WP2.1), dendritic cells (WP2.2), NK- cells (WP2.4) and tumor imaging (WP2.3).
A brief overview of the projects will be provided.

2.O.06

ITCC, THE INNOVATIVE THERAPIES FOR CHILDREN WITH CANCER CONSORTIUM: A PARADIGM FOR PAEDIATRIC EARLY DRUG DEVELOPMENT NETWORKS IN EUROPE?

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ITCC was created in 2003 as a European network to support the introduction of new therapies into the paediatric cancer population. There are two core arms to the network. Firstly a biology programme to evaluate new compounds in a preclinical setting with the aim of prioritising drugs for further clinical evaluation. Secondly a network of clinical centres in Europe able to deliver high quality Phase I and II clinical trials.
To date 9 research laboratories are participating in the biology programme linked by a consortium agreement. These laboratories include specialist units focusing on rhabdomyodsarcoma, Ewings sarcoma and osteosacrcoma. A large biological resource of tumour samples, cell lines and gene profile data is available through this network. The clinical trials programme has identified and accredited 36 centres in 6 EU Member States to conduct clinical trials.
ITCC has become recognised as the major academic network for drug development in paediatric cancer in Europe. Strong collaborations have been forged with the pharmaceutical industry, and regulatory authorities to capitalise on the emerging EU legislation facilitating the development of drugs for children. We are also in a strong position to advise and partner with the major disease-specific groups developing Phase III trials in a range of tumours such that new therapies can be introduced appropriately into front-line treatment.

2.O.07

KIDSCANCERKINOME; KINASE DRUG TARGETS IN PAEDIATRIC CANCERS

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In this lecture I will present an update on the activities of the European KCK (KidsCancerKinome) consortium. Nine European research centers devoted to molecular-biologic, pharmacologic and clinical studies of childhood cancers and two SMEs are engaged in the KidsCancerKinome consortium. The research centers already have an established collaboration for pre-clinical evaluation of anti-cancer compounds in the European 'Innovative Therapies for Children with Cancer' consortium (ITCC).
The KidsCancerKinome consortium aims to perform a comprehensive analysis of the human protein kinase family in childhood tumors, as protein kinases are excellent targets for small inhibitory molecules designed for adult tumors, and many more of such drugs are currently in development. Six aggressive childhood tumors, killing ~2000 children in Europe annually, will be addressed, i.e Ewing sarcoma, osteosarcoma, rhabdomyosarcoma, neuroblastoma, medulloblastoma and ALL.
The KCK consortium has generated gene expression profiles (Affy U133plus2 arrays) of >500 tumor samples form those six tumortypes. We have performed extensive analyses of mRNa expression of human kinases. Examples of interesting expression patterns of the human kinome will be presented.
Detailed analyses for the first 5 kinases for which targetted drugs are available, i.e. PI3K, IGF1R, AURKA+B, and CDK2 will be presented.
Lentiviral shRNA mediated knockdown of kinase protein expression has been used in cell lines to validate those kinases as drug targets.
Many novel kinase inhibitors are under development for adult oncology and KCK will test their in vitro activity against the tumor-driving kinases identified in this program. We are currently testing small molecule inhibitors for the first 5 kinases. For those kinases that have no small molecule inhibitors, a novel generation of siRNA based nucleic acid drugs (LNAs), produced by the Santaris company, will be applied and tested in vitro.
Successful small molecule inhibitors and LNAs will be taken further to in vivo validation in established xenograft models of the six childhood tumor types. Pharmacokinetic studies of these drugs will finally prepare them.

2.O.08

THE EUROPEAN AND AMERICAN OSTEOSARCOMA STUDY GROUP PROTOCOL, EURAMOS-1: SUCCESSFUL TRANSATLANTIC COOPERATION IN OSTEOSARCOMA

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The European and American Osteosarcoma study group (EURAMOS) was formed by four multinational study groups (COG, COSS, EOI, SSG) based upon a common understanding that broad international collaboration facilitating randomised trials was important for further progress in the field of osteosarcoma. Representatives from each group reached quick agreement on a study design; to determine whether altering post-operative therapy based on response to pre-operative chemotherapy improves outcome. Additionally, a quality-of-life sub-study was included in the project. After a three-year process to resolve regulatory and organisational issues the study opened for accrual in April 2005. Important for an efficient conduction of the trial a common infrastructure was established with central sponsorship (Medical Research Council, UK), one coordinating data centre (MRC Clinical Trials Unit, UK) and a common Safety Desk and a coordinating Quality-of-life data centre (Münster, DE).
As of Dec-2008, a total of 1268 patients from 290 institution in 15 countries have been registered into the trial (AUS 16 patients; B 27; CAN 54; CH 26; D 266; DK 12; FIN 3; H 14; NL 61; NOR 23; NZ 8; OST 7; SWE 25; UK 174; USA 552) and 937 patients participate in the quality-of-life evaluation. 697 patients have been randomized and 53% are assessed as good histological responders. Due to a lower than expected randomisation rate and a higher than expected number of patients with a good histological response the accrual time will be extended by one year to summer 2010.
In conclusion, EURAMOS-1 may serve as a model for a successful non-commercial multinational clinical trial in times of increasing economic and regulatory pressure. It is the fastest accruing and largest osteosarcoma trial ever. In addition, to addressing important questions in a randomised setting a common language in osteosarcoma has been established.

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2.O.09

A EUROPEAN TREATMENT PROTOCOL FOR BONE SARCOMA IN PATIENTS OLDER THAN 40 YEARS

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EUROpean Bone Over 40 Sarcoma Study (EURO-B.O.S.S.) is the first prospective multicenter international study for patients 41-65 year old with high-grade bone sarcoma
Patients with HG Osteosarcoma (OS), HG sarcoma NOS (S), Fibrosarcoma, MFH, Leiomyosarcoma, Dedifferentiated Chondrosarcoma (DCh) were included. Chemotherapy: Combinations of cisplatin/doxorubicin (CDP 100mg/m2/ADM 60mg/m2), ifosfamide/CDP(IFO 6g/m2/CDP 100mg/m2) and IFO/ADM (IFO 6g/m2/ADM 60mg/m2) were repeated three times (9 cycles). Surgery was planned after 3 cycles. Methotrexate (8g/m2) was postoperatively added in poor responders. Immediate surgery was allowed and 9 cycles with CDP, ADM, IFO were postoperatively given.
At December 2007, 140 patients were registered (median age 51 years). OS (51%), S (16%), and DCh (11%) were the more frequent histotypes. Synchronous metastases in 30 (21%) patients, central location of tumor in 45(32%).Surgical complete remission (SCR) was achieved in 84% of patients, (localized 91%, metastatic 37%) without difference among the histology groups. One surgical-related and one chemotherapy-related death were reported.
Grade4 WBC and PLT incidence was 55% and 17%.Renal toxicity and peripheral neurotoxicity were reported in 16% and 20% of patients. With a median follow-up of 25 months (4-68) 3 year OS was 58% (95%CI 48-68%) [7% (95%CI 0-19%) without SCR]. In patients with SCR, 3-year OS and EFS were 46% (95%CI 9-83%) and 0% in case of synchronous metastases and 69% (95%CI58-80%) and 45% (95%CI33-57%) for localized patients; 50% (95%CI 29-71%) and 40% (95%CI 20-59%) for patients with central tumor, 73% (95%CI61-85%) and 44% (95%CI31-57%) for those with extremity tumor; 68% (95%CI 52-83%) and 46% (95%CI 32-54%) for OS, 64% (95%CI 42-85%) and 48% (95%CI 25-71%) for S, 48% (95%CI 13-82%) and 27% (95%CI 1-54%) for DCh.
The protocol is feasible, but the chemotherapy-related toxicity is remarkable. Surgical complete remission is the main factor influencing survival. Central location and synchronous metastases are negative prognostic factors, but 50% 3-year OS can be achieved with aggressive local and systemic treatment. Osteosarcoma and high-grade sarcoma NOS benefit from chemotherapy more than patients with dedifferentiated chondrosarcoma.

2.O.10

EUROPEAN CLINICAL RESEARCH INFRASTRUCTURES NETWORK (ECRIN) AS A SUPPORT TO MULTINATIONAL TRIALS

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Clinical research needs distributed infrastructures: efficient patient recruitment is a major bottleneck to clinical research, whereas quality of investigation, credibility of data, and compliance with regulation require professionalized support. The European Clinical Research Infrastructures Network (ECRIN) is designed to support multinational clinical research in the European Union. It is based on the connection of national hubs, each coordinating a national network of generic clinical research centres or of disease-oriented networks. Supported by the European Commission (FP7 Infrastructure programme) as an ESFRI roadmap infrastructure, it promotes multinational collaboration within the European Union, taking advantage of the EU population size and unlocking latent scientific potential.
Building such a distributed, pan-European infrastructure requires addressing the challenge raised by the fragmentation of health and legislative systems. Networking of national clinical research infrastructures led to the development of common standards, of harmonised tools and practice. In addition, ECRIN provides integrated, 'one-stop shop' services to investigators and sponsors in multinational studies: patient recruitment and investigation, quality assurance, monitoring, ethical and regulatory requirements, adverse event reporting, circulation of medicinal products and of blood and tissue samples, data management. Information and consulting also help investigators prepare their study: ethical and regulatory requirement, insurance, centre selection, cost evaluation, funding opportunities. Access is given to users (mostly investigators and sponsors in the academic institutions that often lack the capacity to act as a sponsor in the conduct of EU-wide studies) after assessment of the protocol by the scientific board. Services provided by ECRIN are particularly relevant for research on rare diseases and neglected diseases, for clinical trials in elderly and paediatric populations, for academic clinical research institutions, and for clinical trials steered by biotechnology SMEs.

2.O.11

ESF-EMRC FORWARD LOOK INVESTIGATOR-DRIVEN CLINICAL TRIALS: KEY RECOMMENDATIONS FOR STRENGTHENING PATIENT ORIENTED RESEARCH IN EUROPE

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Investigator-Driven Clinical Trials (IDCT) form a key part of patient-oriented clinical research, the basis for continually improving patient care. Such research is under strain in Europe for a multiplicity of reasons, and because of this the European Medical Research Councils (EMRC) of the ESF has undertaken in 2007 a Forward Look exercise. This Forward Look represents what is probably the most comprehensive examination of IDCT in Europe in recent years. A thorough analysis of the problems faced by academic investigators conducting IDCT was carried out through a series of workshops covering different themes and attended by active and acknowledged experts in the field. These workshops identified specific issues that need to be addressed:

- Categories and Design of Investigator-Driven Clinical Trials
- Regulatory and Legal Issues, Intellectual Property Rights and Data Sharing
- Management of Investigator-Driven Clinical Trials
- Education, Training, Career Tracks and Authorship
- Funding and Models of Partnership
- Status of Investigator-Driven Clinical Trials in Central and Eastern European Countries

A range of possible solutions were proposed and five among the 26 recommendations as ranked by the consensus conference, held on 29-30 September 2008, were considered as top priorities to strengthen IDCT in Europe:

1. To improve the education, training and career structure for scientists involved in patient-oriented clinical research.
2. To increase levels of funding for IDCT.
3. To adopt a ‘risk-based’ approach to the regulation of IDCT.
4. To streamline procedures for obtaining authorisation for IDCT.
5. To ensure that IDCT are carried out with an appropriate number of patients to produce statistically reliable results – that the trials are ‘correctly powered’.

To help implement the recommendations expressed in the report for strengthening patient oriented research in Europe a broad dissemination to the four stakeholder groups identified as key players will be assured.We clearly think that if we can collaborate on this important issue and improve conditions for clinical research, we can contribute to bringing better health and prosperity to Europe.

3.O.01

CLEAR-CELL SARCOMA – A REVIEW OF A SOFT-TISSUE SARCOMA WITH FATAL PROGNOSIS

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Clear cell sarcoma (CCS) is a rare and highly malignant soft-tissue sarcoma (STS) constituting 1% of all STS. It most often appears in the soft tissue closely associáted with tendons, aponeuroses or fascial tissue of the distal extremities. It shares features of melanomas, hence is dubbed as a soft-tissue melanoma or clear cell sarcoma of the tendons and aponeuroses (CCSTA). CCS differs from the more common STS by its more aggressive growth and greater propensity to metastasise to lymph nodes, bones and lung. On a molecular basis, CCS is characterised by the chromosomal translocation.
Clinically, the tumor is firm, slowly growing and painless in half of the cases, thus rarely awakening suspicion of a STS. Thus, the diagnosis is difficult. Furthermore, on an MRI the tumor exhibits mostly a homogenous mass with a higher signal intensity as compared to muscle on T1-weighted images and implies a benign tumor.
The most important treatment is a wide resection to ensure local control. Little is known about neo- and/or adjuvant chemotherapy or radiation. Regarding chemotherapy different substances (doxorubicin, ifosfamide, cisplatin, mesna, dacarbazine, cyclophos-phamide) have been administered under different conditions (single or combined substances, different doses, neo- or adjuvant). There are also some reports displaying the advantages of caffeine-assisted chemotherapy.
Under similar different circumstances radiation therapy was applied.
Most important prognostic factors are the presence of tumor necroses, size and regio-nal lymph node metastases, local recurrence and distant metastases.
The reported 5-year survival ranges from 48% to 68%, the 10-year survival from 36% to 41%.
Summarising all reports there is a need at least for a retrospective study to gather information about more patients.

3 .O.02

HAEMANGIOENDOTHELIOMA OF BONE; DOES IT EXIST?

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Over the years, the terminology and classification of vascular tumors of bone has been highly controversial and in literature a great variety of names has been proposed. The large variety of entities of vascular tumors of bone suggests that it should be regarded as a spectrum with on one side the overtly benign lesions and on the other side the frankly malignant lesions. In between there is the intermediate category in which numerous histomorphological diversity can be seen and for which classification is most difficult. Benign vascular lesions of bone (solitary haemangiomas) at the one end of the spectrum, are relatively common and occur most frequent as an asymptomatic incidental finding in the skull or spine, although extraspinal locations are also reported. At the other end of the spectrum, primary malignant vascular tumors of bone are rare, representing less than 1% of primary malignant bone tumors.
Angiosarcoma is the most acceptable term for high-grade malignant vascular tumors of bone, which is highly aggressive with an ominous prognosis. The classification of the intermediate category of vascular tumors of bone, in particular of so-called haemangioendotheliomas, is extremely difficult due to the lack of uniform terminology and accepted histological criteria. Many authors have proposed different classification systems, but due to small numbers of cases, their large diversity and the lack of good correlation with clinical outcome none of them have been generally accepted so far. Within this intermediate category, epithelioid hemangioendothelioma is a separate and well recognized entity with morphological features exactly similar to its soft tissue counterpart, and is often multifocal.
Epithelioid hemangioma is a recently described entity characterized by a moderately differentiated, lobulated proliferation of epithelioid endothelial cells. The lesion can be multifocal, and behaves in a benign fashion although local recurrence (8%) and spread to the lymph nodes (2%) may occur. There is considerable overlap with the entity previously described as haemangioendothelioma of bone which has variable histological patterns and no distinguishing histological features could be proposed. Moreover, the entity hemangioendothelioma of bone may not only overlap with epithelioid hemangioma of bone, but also with the rare low grade angiosarcoma of bone. Therefore, there is increasing evidence that haemangioendothelioma of bone seems to represent two different entities and the use of this term should be avoided.

3.O.03

MOLECULAR AND IMMUNOHISTOCHEMICAL CHARACTERIZATION OF BONE AND SOFT TISSUE EPITHELIOID HEMANGIOENDOTHELIOMA

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Epithelioid hemangioendothelioma (EHE) is a rare vasoformative tumor of variable biological behavior that has been considered a tumor of borderline malignancy and low-grade angiosarcoma. The majority of cases are associated with low mortality, but some metastasize and cause patient death. Its principal sites of occurrence are soft tissues, liver, lung, and bone. EHE develops as a solitary, painful mass in superficial or deep soft tissue of the extremities and it generally arises from a vessel. Cytogenetic findings are very limited and comprises three reports on totally 4 cases, describing translocations between chromosomes 1 and 3 in two cases, chromosomes 7 and 22 in one case and chromosome 10 and 14 in the last case.
We characterized immunohistochemically 5 cases of this tumour type and currently we are performing Real-Time PCR assays to analyze the expression of two genes (MDM2 and CDK4) known to be involved in pathogenesis of tumours.
Three out 5 patients presented epithelioid hemangioendothelioma of the bone while two affected soft tissues. All the samples showed positivity for CD34 and CD31; 4 samples out 5 were also positive for FLI1. We tested Factor VIII immunostaining on 3 of these cases which resulted positive; EMA was positive on 3 samples out 5. Cytocheratins (AE1/AE3, CAM 5.2 and CK7) were always negative except in one case which showed CAM 5.2 positivity. Our preliminary results by Real-Time PCR analysis performed on 5 cases suggest that MDM2 and CDK4 have a different expression in epithelioid hemangioendotheliomas compared to normal tissue.
Our study shows that use of molecular techniques such as Real-Time PCR could complement histopathological diagnosis in order to identify a marker of biologic behaviour of this enigmatic tumour type.

3.O.04

HEMANGIOENDOTELIOMA OF BONE: A REVIEW OF THE RIZZOLI EXPERIENCE

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University of Bologna, Istituto Ortopedico Rizzoli, BolognaForty-six hemangioendotheliomas (HE) of bone treated at Rizzoli from 1985 to 2004 were studied with minimum follow up of 4 years: 19 females and 27 males, mean age 37 years, mean follow-up 9 years, 35 cases unifocal at diagnosis (10 spine - 1 with lung metastasis also- 11 lower limb, 8 upper limb, 6 pelvis) and 11 with multifocal involvement. In 10 patients intralesional surgery was previously performed elsewhere. In 27 patients primarily treated at Rizzoli with unifocal localization, surgery was used in 15 cases, surgery and radiotherapy in 7, surgery with radio/chemotherapy in 1 and no surgery in 4 (2 radiotherapy, 1 radio/chemotherapy and 1 embolization). Eight unifocal patients already treated elsewhere had surgery in 3 cases, surgery and radiotherapy in 3, surgery with radio/chemotherapy in 1 and surgery plus chemotherapy in 1. Three of the unifocal cases had further bone involvement subsequently. Nine multifocal patients primarily treated at Rizzoli had surgery in 4 cases, surgery and radiotherapy in 4, surgery with radio/chemotherapy in 1. The 2 previously treated multifocal HE had 1 surgery and 1 radiotherapy.
Six patients died: 3 of disease, 1 of radio-induced osteosarcoma, 2 of different disease. Two patients are AWD. Of remaining 40 patients, 26 are NED (mean follow up 9 years), 11 NED after treatment of recurrence, 1 NED after treatment of radio-induced sarcoma. No lung metastases were diagnosed after treatment. All 10 cases previously treated intralesionally had recurrence. Two of 15 unifocal cases treated with surgery recurred (13%). None of 9 resected unifocal cases previously untreated recurred. Two of 21 pts. with radiotherapy (9.5%) had radio-induced sarcoma.
Surgery is recommended, resection when feasible. Radiotherapy, implying risk of induced sarcoma, should be reserved to multifocal or unresectable cases. Adverse prognostic factor was previous intralesional surgery.

3.O.05

HIGH-GRADE ANGIOSARCOMA OF BONE: A CLINICOPATHOLOGICAL STUDY OF 64 CASES

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High-grade angiosarcomas (HGAS) of bone are rare and represent less than 1% of the primary malignant bone tumours. Because of their rareness little is known. Clinically, it is accepted that they are extremely aggressive. Due to the lack of uniform terminology and accepted histological criteria, terminology and classification of primary malignant vascular tumours of bone has been highly controversial. Today, angiosarcoma is the most accepted term for high-grade primary vascular tumour of bone, recognized by the 2002 WHO Classification. However, distinct histological hallmarks to define a HGAS of bone are not clear.
We collected 64 HGAS of bone diagnosed between 1964 and 2007 from the files of the departments of pathology, Leiden University Medical Center (Leiden), Rizzoli Institute (Bologna) and University Hospitals (Leuven). All clinical, radiological, and pathological data were reviewed and different histological criteria were scored. A tissue micro-array was constructed containing 57 HGAS of bone. To confirm the vascular origin of all lesions and to investigate the diagnostic value of commonly used markers, immunohistochemistry was performed for CD31, CD34, Factor VIII, and keratin AE1/AE3. Staining was evaluated positive or negative.
Among 64 patients with HGAS of bone, there are 41 males and 23 females. There is a wide age distribution, with a nearly equal distribution from the second to the sixth decade. The solitary cases are mostly located in the extremities (66%) followed by trunk (12.8%), axial/central location (10.6%) and pelvis (10.6%). 17 cases (73%) have multifocal bone lesions. HGAS of bone show variable histological patterns. Association with clinical outcome (chi-square test) reveals that there is a significant poor survival when the tumour has tree or more mitoses ($p=0.001$), a macronucleoli ($p=0.011$) or there is an absence of an eosinophilic infiltrate ($p=0.023$). The HGAS of bone are positive for CD31 in 53/55 (96%), CD34 in 33/57 (58%), Factor VIII in 47/55 (86%), and keratin in 40/57 (70%). Only 15 out of 40 (38%) keratin positive angiosarcomas, showed an epithelioid phenotype at classical morphology. All tumours with an epithelioid phenotype are keratin positive.
Although HGAS of bone in general have a poor outcome, histological criteria such as three or more mitoses, the presence of a macronucleolus and the absence of an eosinophilic infiltrate can be useful to predict a more aggressive course, consistent with the clinical behaviour of a high-grade angiosarcoma. CD31 and Factor VIII are the best diagnostic markers for HGAS of bone. It is striking that keratin positivity is seen in the majority of cases, and is independent of epithelioid morphology. Pathologists should be aware of this to avoid misinterpretation as metastatic carcinoma.

3.O.06

GORHAM SYNDROME IN THE PELVIS: CASE REPORT AND LITERATURE REVIEW

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Gorham syndrome is a rare disease of unknown cause. It is characterized by the massive bone destruction associated to bone angiomatosis. It was first described by *Jackson* in 1838. *Gorham and Stout* published their initial report in the fifth decade of the last century. The diagnosis depends on the exclusion of other diseases that cause bone lysis. The treatment has no uniformity between the oncologists, and different modalities of therapeutic procedures are being used as radiotherapy, biphosphonates, interferon and surgery.
This case reports a man, 44 years old, caucasian farmer that had a progressive pain in the left groin one year ago. The pain was getting worst and migrated to the left hip. A pelvis X-ray revealed isquiatic lysis with total disappearing of the bone. The left hip presented diffuse lytic areas too. The clinical profile of the patient was good and it was discrepant when compared to the X-rays with bone destruction .The investigation was done with bone scintilography, MRI of the pelvis, computed tomography (CT) of abdomen and chest, blood analysis of PTH, calcium, phosphate, eletrophoresis of proteins, PCR, hepatic function, and two consecutive bone biopsies of the left hip and pelvis. All exams excluded metastatic or primary bone tumors. A multidisciplinary team of clinical oncologists, endocrinologists, nephrologists excluded other neoplastic, metabolic and rare diseases as Hadju and Cheney acro-osteolysis, carpal and tarsal osteolysis, multicentric osteolysis with nephropaty, hereditary multicentric osteolysis, Joseph acro-osteolysis, Shinz acro-osteolysis, Faber disease and Winchester disease. A multidisciplinary meeting decided by the orthopaedic surgery and radiotherapy to relieve the pain and to achieve the pathological diagnosis. The girdlestone surgery was done and the histopathological analysis showed diffuse angiomatosis in the specimen, diagnosing Gorham syndrome.
Gorham syndrome diagnosis depends on a *tripod*: clinical exclusion of other pathologys, image investigation and histopathology diagnosis. All three characteristics are primordial to the diagnosis of this pathology and a full investigation in a multidisciplinary level is necessary.

3.O.07

GORHAM-STOUT DISEASE: THE EXPERIENCE OF ISTITUTO RIZZOLI

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Gorham-Stout disease (GSD) is rare, characterized by proliferation of vascular channels resulting in progressive distruction of bone. In the Rizzoli files we found 15 cases of GSD from 1968 to 2008. Two were excluded for insufficient documentation. For 13 cases clinical data, imaging and histology were analysed. Histopathologic features included benign vascular proliferation, vascular pattern of osteolytic angioma, fibro-connective tissue component and bony destruction. A final diagnosis was established based on clinical, radiological and histopathologic features.
Imaging included X-rays in 11 cases and CT or MRI in 5. All lesions were lytic, with associated sclerosis in two cases. There was one lesion only in 4 cases, multiple lesions in the same bone in 1 and multiple bones involved in 6. Primary sites were proximal femur in 7 cases, pelvis in 2, hip and knee, calcaneus, humerus and cervical spine in 1 case each. Two patients had no treatment, 2 conservative treatment (cast or brace), 5 surgery, 6 medical treatment (byphosphonates, calcitonin, zoledronic acid, interferon, steroids), 1 radiotherapy, 2 selective arterial embolization. Surgery consisted of internal fixation of pathologic fractures in 4 patients and reconstruction of the entire humerus with a double composite allograft in 1. Treatment was surgery only in 2 patients, medical treatment in 4 (1 also embolization), surgery and medical treatment in 2 (1 also embolization), radiotherapy only in 1, conservative treatment in 2. Four patients were lost at follow up. Mean follow up was 17 ys.(min 2, max 30) in 9 patients: 2 dead, 3 healed, 3 with stable disease, 1 alive with disease at 24 ys.
No conclusive treatment recommendations are possible; surgery is indicated in pathologic fractures or reconstruction of massively destroyed bones, medical treatment and selective embolization are helpful. In literature prosthetic reconstruction is preferred due to the risk of allografts resorption.

3.O.08

ESTABLISHMENT OF THE CHICK CHORIO-ALLANTOIC MEMBRANE ASSAY FOR GIANT CELL TUMOR OF BONE

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Because of the lack of a suitable *in vivo* model for giant cell tumors of bone little is known about their biological behavior and mechanisms of metastasis. No existing cell line contains all tumor components, so that testing of anti tumor agents is hardly possible. We therefore modified the chick chorio-allantoic membrane (CAM) assay for giant cell tumor of bone (GCTB).
Out of tumor tissue obtained during surgery of 5 patients a solution was produced. The solute was grafted onto the CAM at day 10 of embryonic development. The growth process was monitored by daily observation and photo documentation using *in vivo* microscopy. After 5 to 6 days of tumor growth the samples were fixed in formalin and further analyzed using standard histology (hematoxylin and eosin stains).
The tissue solute of all 5 patients formed solid tumors when grafted to the CAM. *In vivo* microscopy and standard histology revealed a rich vascularisation of the tumors. The tumors were composed of the typical components of GCTB including multinuclear giant cells.
A reliable protocol for grafting of human giant cell tumors onto the chick chorio-allantoic membrane was established. This model is the first *in vivo* model for giant cell tumors of bone. Further characterization of the growing tissue is necessary in further experiments.

3.O.09

VIVO AND IN VITRO EFFECTS OF BISPHOSPHONATE TREATMENT ON GIANT CELL TUMOUR OF BONE

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Giant cell tumour of bone (GCTB) is an expansile osteolytic tumour of bone which contains numerous osteoclast-like giant cells. GCTB is a locally aggressive tumour which can cause extensive bone destruction that can be difficult to control surgically, up to 35% of cases recurring after simple curettage. Bisphosphonates are anti-resorptive agents that have proved effective in the treatment of a number of osteolytic conditions.
In keeping with its known effect on osteoclasts, we found that the aminobisphosphonate zoledronate abolished in vitro lacunar resorption in cultures of osteoclasts isolated from GCTB. The effect of zoledronate and other bisphosphonates on 15 cases of recurrent primary GCTB, four of which had metastasised to the lung, was assessed clinically. Most recurrent tumours did not exhibit progressive enlargement and, in some cases, both primary and metastatic GCTBs showed a degree of radiological improvement following treatment However, tumours did not diminish in size and, in some cases, no apparent treatment effect was noted.
Our findings provide in vitro evidence for the use of bisphosphonates to inhibit the progressive osteolysis associated with GCTB. In vivo, these agents produced a degree of clinical and radiological improvement in some cases. This study reports results from three European centres where bisphosphonates are being used to treat recurrent GCTB and highlights the fact that these centres are all employing different clinical indications and different regimes of bisphosphonate treatment. Bisphosphonates have significant side effects and indications for treatment and standardisation of drug type and dosage regimes (and measurement of agreed outcome measures to determine treatment efficacy) should be established before these agents are included as part of a treatment protocol to control GCTB tumour growth and osteolysis.

3.O.10

INCIDENCE, PREDICTIVE FACTORS AND PROGNOSIS OF CENTRAL CHONDROSARCOMA IN PATIENTS WITH OLLIER DISEASE AND MAFFUCCI SYNDROME; REPORT OF 133 PATIENTS

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Enchondromatosis is a non-hereditary disease, characterised by the presence of multiple enchondromas. While Ollier Disease is typified by multiple enchondromas, in Maffucci Syndrome they are combined with haemangioma.
Due to the rarity of these diseases, systematic studies on clinical behaviour providing information how to treat patients are lacking.
This study intends to answer the following questions: What are predictive factors for developing chondrosarcoma? When is extensive surgery necessary? How often patients die due to dedifferentiation or metastasis?
Twelve institutes in eight countries participated in this descriptive retrospective EMSOS-study. 118 Patients with Ollier Disease and 15 patients with Maffucci Syndrome were included. Unilateral localization of disease was found in 60% of Ollier patients and 40% of patients with Maffucci Syndrome.
One of the predictive factors for developing chondrosarcoma is the location of the enchondromas; the risk increases especially when enchondromas are located in the scapula (33%), humerus (18%), pelvis (26%) or femur (15%). For the phalanges, this risk is 14% in the hand and 16% in the feet. The decision whether or not to perform extensive surgery is difficult, especially in patients who suffer multiple chondrosarcomas.
Malignant transformation was found in fourty-four patients with Ollier Disease (37%) and eight patients with Maffucci Syndrome (53%). Multiple synchronous or metachronous chondrosarcomas were found in 15 patients.
Nine patients died (range 21-54 yrs). Seven of them died disease related due to pulmonary metastasis (2 humerus, 2 pelvis, 3 femur). Two patients died from glioma of the brain.
In conclusion, one important predictive factor for developing chondrosarcoma is the location of the enchondromas; interestingly, only patients with chondrosarcoma outside the small bones died of their disease. In this series, no dedifferentiation of chondrosarcoma was seen. A first design flow-chart how to approach chondrosarcoma in patients with Ollier Disease and Maffucci Syndrome is in preparation.

3.O.11

EXTRATHORACIC SOLITARY FIBROUS TUMOUR: A RARE ENTITY WITH AN UNPREDICTABLE BEHAVIOUR

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Solitary fibrous tumour (SFT) is a relatively uncommon mesenchymal neoplasm that most frequently arises in the pleura, but is also known to affect extrathoracic sites. About 15 % of SFT's behave in an aggressive way, giving rise to local recurrence and/or distant metastasis. However, the behaviour of SFT remains unpredictable and due to the rarity of this tumour, it is difficult to define prognostic factors. The purpose of this study was to describe our experience with SFT, trying to define the pathologic features of this rare entity and better understand its clinical behaviour.
We performed a clinicopathologic review of all cases treated for a SFT at the Istituto Ortopedico Rizzoli in Bologna, between 1996 and 2008. We included 24 patients, nine males and fifteen females, ranging in age from 22 to 82 years (median 43.5 years). The anatomical sites involved were: the thigh (12 cases), shoulder region (four cases), gluteus (three cases), foot (two cases), extrapleural thoracic wall (two cases), and the lower leg (one case).
The tumour was >5 cm in 15 cases, ranging in diameter from 2.5 cm to 18 cm (median 7.5 cm). Pain and swelling were the most frequently reported symptoms at presentation, with a mean duration of symptoms of 10 months. All patients were treated by excisional surgery (wide margins in 11, marginal margins in 13). Three patients had undergone pre-operative radiotherapy (44Gy) and one of these had also adjuvant radiotherapy after marginal excision of the tumour. Six tumours showed at least one atypical histologic feature (moderate to marked cytological atypia, extensive tumor necrosis, ≥ four mitoses per ten high-power fields, or infiltrative margins). On immunohistochemistry, 21 cases were positive for CD-34, 10 for CD-99, 17 for vimentin, three for CD-31, four for actin and one for S-100. Subsequent follow-up (average 33 months, range 5 to 112 months) revealed tumour relapse in only one case: a bone metastasis after 36 months of follow-up. The initial lesion was considered a large, deep, malignant SFT of the thigh, treated with wide surgical excision.
In the current review, including 24 extrathoracic solitary fibrous tumours, all lesions but one had a benign course. Nevertheless, this entity has a potential to recur or metastasize, and therefore careful long-term follow-up is necessary for all patients, even after wide excisional surgery. Although specific prognostic factors are yet to be defined, a high degree of suspicion for malignant behaviour is warranted for those cases in which atypical histologic features are present, particularly in the context of a deep tumor > 5cm in diameter.

3.P.01

INTERFERON α–2b TREATMENT FOR CHILDHOOD PRIMARY AND RECURRENT HEMANGIOENDOTHELIOMA OF BONE

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Hemangioendothelioma is a rare vascular tumor that is infrequently recognized in bone. It can be multicentric and often painful with an indolent course. The treatments of choice include curettage, resection, radiation, systemic medications or a combination of these modalities.
O.G. 5 years old girl, presented with left ankle pain and limping , without response to non steroidal anti-inflammatory drugs for few months. Radiological investigation (MRI) showed a lytic vascular lesion in the methadiaphysis, invading the epiphysis of the distal left tibia and lateral cartilage of the ankle, with atrophy of the left lower limb. Bone scan showed high uptake in this area. Histology showed fragments of bone, infiltrated by a vascular lesion with nodular pattern, well differentiated vascular spaces and endothelial cells with few mitotic figures. Immunostains were positive for CD31 and F8. The pathology report confirmed hemangioendotAs the lesion invaded the growth plate of the distal tibia, surgical or radiation therapy at this age could cause a permanent damage. We therefore successfully treated the child with Interferon b 0.5 million IU three times a week for 18 months. She was pain free after the first few months of therapy with full recovery of daily function and activity. Radiological evaluation showed improvement on X-ray and MRI, and shrinkage of the lesion to the epiphysis area only.
Unfortunately, 3 years later the pain and limping reappeared. MRI showed a lytic lesion in the diamethaphysis of the left tibia. Re-biopsy supported the diagnosis of recurrent hemangioendothelioma. She was retreated with Interferon α–2b using the same protocol with considerable improvement of the pain and limping.
We present here a non invasive option for therapy with Interferon α–2b for bony lesion of hemangioendothelioma that enable us to spare the growth plate in a growing prepubertal child.

3.P.02

EPITHELIOID HAMANGIOENDOTHELIOMA (EH) OF THE HAND: REPORT OF TWO CASES

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EH of bone is a rare vascular neoplasm, subtype of hemangioendothelioma, characterized by mesenchimal cells that have an epithelioid endothelial appearance. There are different kinds of EH: the benign epithelioid hemangioma, and the malignant epithelioid angiosarcoma.
This tumors can occurs in soft tissue, lung, liver and bones and often are multicentric.
EH generally involve the bone of the spine and lower limb and is very rare in the upper limb and the hands. The main symptom is pain; pathological fracture may occur in aggressive lesions.
Radiographically the EH is a ostelytic lesion with variable peripheral sclerosis, cortical destruction and periosteal new bone.
Treatment of EH is curettage and local adjuvants in benign lesion, en bloc resection in the low-grade forms and wide or radical surgery in the high-grade forms. Radiation therapy is suggest in inoperable situations.
In the present report we describe the clinical features, the oncological treatment and the reconstructive solutions of two cases of EH of the hand treated in the Orthopedic Oncological Center of Gaetano Pini Institute of Milan. Both cases had multiple locations in the carpus, metacarpus and phalanges. The involvement of more joints caused a delayed diagnosis (> 1 year). Exeresi and reconstruction of several segments of the wrist and hand has led to considerable technical difficulties resolved with the collaboration of the microsurgeon and plastic surgeon.

3.P.03

INTRAMUSCULAR CAVERNOUS HEMANGYOMA OF THE THIGH

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Intramuscular hemangyomas are benign tumours (0,8% of all hemangyomas). Their aetiology is uncertain but they are possibly congenital, although some seem to be related to trauma. Symptoms (usually pain and swelling) may be present for years. Histological subtypes are cavernous, capillary and mixed. Optimal management includes precise diagnosis and wide excision to prevent local recurrence.
Authors present a case of a 79 years male with cavernous hemangyoma of the thigh with three years of evolution. The tumour eroded the femur and the patient had a mass all over the thigh with tension and pain. Diagnosis was suspected by phleboliths seen on x-ray and MRI and was confirmed by open biopsy.
Treatment was a complete excision with double approach, medial and lateral, plus prophylactic nailing of the femur.
With a four years follow – up, the patient has no sign of recurrence and has a normal function of the inferior limb and a normal gait.

3.P.04

TWO CASES OF EPITHELOID HAEMANGIOENDOTHELIOMA WITH BONE INVOLVEMENT

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Epitheloid haemangioendothelioma is a rare tumour of vascular origin. It is characterised by the appearance of epitheloid endothelial cells and occurs typically in soft-tissue, skin, and liver. Less frequently it is found in bone. The tumour is more often located in the long bones of the lower extremities, and the pelvis than in the upper extremities, vertebral column, and flat bones. The lesion nearly affects all age groups and there is a male predilection.
Case 1: A 71-year old woman had pain in the area of her right hip after a downfall. X-ray showed a lucency of the cortical substance of the right femur. Scintigraphy showed a cortical lesion, oedema of the bone-marrow and an involvement of soft-tissue. Carcinoembryonic antigen, CD 31, and CD 8 were positive. An open biopsy verified an epitheloid haemangioendothelioma. Staging was negative. A wide resection of the proximal femur and reconstruction with a tumour-prosthesis were performed. Four months later the patient had osteolytic metastases of os ilium, os pubis, acetabulum and in the fifth lumbar vertebra. The patient died 8 months after the wide resection of the tumour because of myocardial infarction.
Case 2: An epitheloid haemangioendothelioma of the liver was diagnosed in a 21-year old male patient. Twelve years after the primary tumour the patient had osteolyses of the first cervical vertebra, manubrium sterni, and ribs. An open biopsy verified the metastatic spread. Local radiotherapy was performed. Furthermore the patient developed a destruction of processus spinosus and a pathologic fracture of first thoracic vertebra. The patient died of metastatic disease 2 years later or 14 years after the initial diagnosis.
Epitheloid haemangioendothelioma of bone is a rare tumour and the diagnosis is quite difficult. Metastatic rate is about 20-30% and mortality about 10-20%. As presented in our cases bone involvement could either be attributed to primary haemangioendotheliomas of bone or to metastases of non-osseous forms. As in our cases it has been reported, that predicting prognosis is difficult, however nuclear atypia, mitotic activity, spindling of cells, and necrosis have been reported as negative prognostic factors.

3.P.05

WIDE RESECTION WITH POSTOPERATIVE IRRADIATION IN THE TREATMENT OF HAEMANGIOENDOTHELIOMA OF BONE

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Haemangioendothelioma of bone is a rare intermediate grade malignancy. Because of its rareness there is a lack of information in the literature about the well established treatment strategies depending on series with large numbers. The outcome of wide resection with postoperative external irradiation would be presented.
4 patients (2 females, 2 males) with a mean age of 40.5 (26-52) with solitary haemangioendothelioma of bone admitted with local pain on the affected bone and limited restriction of function. Anatomical sites were scapula, calcaneum, midshaft of radius and metaphysodiaphyseal region of femur. Plain X-ray, CT, MRI, Tc 99 tecnetium wholebody bone scan investigations were applied. All lesions were hot on bone scan and lytic irregular permeative lesions T1 hypo, T2 hyper with gadolinium enhancement were present. Open biopsy resulted with the diagnosis of intermediate haemangioendothelioma of bone. Wide resection of tubular bones and intercalary lyophilised allograft recostruction with IM rod and cerclage wire and total calcaneum resection and allograft replacement with talar arthrodesis, total scapulectomy subsequent autoclaved bone reimplantation were the surgical procedures applied. Mean follow-up was 96 months (40-132). Three patients except scapula case received 50 Gy external irradiation. No patient developed local recurrence in the follow up. Regarding complications calcaneum patient developed skin necrosis after the irradiation which led to removal of the allograft but eventually healed. Scapula patient had late infection treated by antibiotics. All patients had satisfactory function. Intercalary allografts united in 6 months time. Calcaneum patient developed multiple small lung metastasis 1 year after the operation and treated by adriamycin based chemotherapy and interpherone. The lung lesions showed slight regression but the patient is alive since 112 months with no further relapse.
Wide excision with subsequent irradiation and wide excision of total scapula resulted with no local recurrence in our small group of patients with this rare malignancy. Irradiation provided relatively less soft tissue sacrification and a sufficient local tumour control without risking the patient to an impending amputation in the occurence of local recurrence.

3.P.06

HAEMANGIOPERICYTOMA OF BONE: REAL OR IMAGINED?

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Haemangiopericytoma (HPC) was first described by Murray and Stout as a soft tissue neoplasm with distinct morphologic features, presumably composed of pericytes. Over the years, it became clear that many tumours could mimic a HPC-like pattern. These days, it is accepted that in soft tissue most lesions diagnosed as HPC in the past are actually solitary fibrous tumours (SFT), synovial sarcomas (SS) or myofibromatoses. It has been unclear whether the very rare HPC of bone is a true entity, or that the HPC-like vessels are non-specific and part of other, different entities.
We collected 10 primary HPC of bone from four institutions diagnosed between 1952 and 2002. All data were reviewed. Immunohistochemistry was performed for CD31, CD34, factor VIII, SMA, keratin AE1/AE3 and EMA. Staining was evaluated as focal positive, diffuse positive or negative.
There were five female and five male patients between 21 and 73 years of age (mean 45.3 y). All tumors were located within bone. The primary site of the tumour was the femur in two patients, humerus in one, fibula in one, sacrum in two and vertebra in three. All tumours showed the presence of prominent thin-walled branching vessels surrounded by more undifferentiated spindle or round cells. However these cells showed some variation in their morphologic pattern: five tumours showed a patternless architecture and varying cellularity, consistent with SFT. Three tumours showed more densely packed sheets of poorly differentiated cells, similar to SS, and one case each represented paraganglioma and PEComa, possibly metastatic. Tumours resembling SFT showed usually focal to diffuse staining for CD34. All tumours were negative for SMA. Two tumours more similar to SS showed focal positive staining for keratin AE1/AE3 or EMA (66%). Some tumours showed severe decalcification artefact. None of the 10 tumours show CD31 and factor VIII expression. FISH is performed to study SYT rearrangements.
Our retrospective review of tumours diagnosed as HPC of bone in the past revealed the absence of true pericytic differentiation and the existence of both SFT of bone and SS of bone. Therefore, as in soft tissue tumours, HPC-like features are non specific. Diffuse CD34 staining is helpful to diagnose SFT of bone, whereas keratin/ EMA staining is suggestive for SS of bone.

3.P.07

HOW TO TREAT VANISHING BONE SEGMENTS?

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Aneurysmal bone cysts are benign lesions of bone that tend to recur if they display an aggressive behaviour. In this study, an aggressive lesion is described as one with almost completely lost cortices on standard x-rays, mimicking 'vanishing bone disease'. Purpose of this study is to retrospectively analyse the treatment results in this special patient subgroup.
Sixteen patients with a mean age of 23.1 (6-44) were included in this study. Femur (%25) was the most commonly affected bone. Spinal lesions were excluded. All lesions were diagnosed by preoperative tru-cut biopsy, however open biopsy was also done if requested by the pathologist. All lesions were preoperatively examined by contrast enhanced MRI. They were evaluated as having almost no cortical bone rim but a periosteum like soft tissue envelope. Intraoperatively, following an extended curettage, this tissue was observed as an alive periosteal layer. Phenolisation was added and cavities were filled with allograft bone chips. The periosteum was sutured around the grafts. Additional stabilisation was performed by external fixator in 3 patients, dynamic compression hip screw in 1.
Patients were followed up for a mean period of 47.8 months (9-84). Lesions healed after a mean period of 28.2 weeks (6-126). There was recurrence in 5 patients. The number of additional procedures necessary for relapsed lesions was 3 for one patient, 2 for another patient and 1 for the remaining 2 patients. Time to healing was not included for 1 patient who refused surgery for relapse and another patient who recently underwent surgery for relapse. One patient healed with a deformity.
Aneurysmal bone cysts may present as highly aggressive local bone lesions. Even in such a subgroup, resection to prevent relapses seems an exaggerated procedure. Extended curretage and packing may yield satisfactory results, with acceptable recurrence rates.

3.P.08

LYMPHANGIOMATOSIS WITH SKELETAL INVOLVEMENT – AN ORPHAN DISEASE LONGING FOR THERAPY

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Vascular anomalies with skeletal involvement are rare. To ameliorate diagnostics and therapy the classification of the International Society for the Study on Vascular Anomalies (ISSVA) should be applied where proliferating vascular tumours are separated from malformations, which are hereditary and do not change. Furthermore, blood and lymph vessel lesions are distinguished. In addition to isolated local or multifocal bone lesions, involvement of soft tissue and/or other organs can be observed.
Here, we report on 6 patients with lymphangiomatosis. Diagnostic workup using whole body MRI is most sensitive to detect all lesions. Localisation was the mandible (n=2), spinal column (n=4), femur (n=1), tibia (n=1), pelvis (n=1), humerus (n=1), scapula (n=1) and rips (n=1). Soft tissue involvement was observed in all patients, 1 patient showed additional lesions in the kidney and spleen, 3 patients in the lung. These 3 patients could be diagnosed with Gorham's disease, a potentially lethal form of skeletal lymphangiomatosis, with thoracic involvement.
Next to the difficulty to find the correct diagnosis, therapy is not standardized. A major problem is the treatment of Gorham's disease. In the literature, case reports on surgery as well as interferon alpha, chemotherapy, bisphosphonates and radiation therapy can be found. We performed surgery (n=2), radiotherapy (n= 1), polychemotherapy (n=1), bisphosphonates (n=2) and conservative therapy (n=3). One of the patients with Gorham's disease died because of progressing pulmonary insufficiency.
It is still unclear if prophylactic therapy for skeletal involvement should be administered and which therapy is effective. An international register and a multicenter clinical trial are urgently needed.

3.P.09

FAILURE OF LIMB SALVAGE FOR DISAPPEARING BONE DISEASE IN THE LOWER LIMB – A REPORT ON TWO CASES

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Disappearing bone disease is also known as vanishing bone disease, phantom bone disease, massive osteolysis, Gorham's disease or Gorham-Stout disease. Basically, it is characterised by osteolysis in (contiguous) bone segments, due to localised proliferation of thin-walled vascular channels in the bone and surrounding soft tissues.
The etiology and pathophysiology of this condition remain poorly understood and largely unclear, but there is increasing evidence that disordered lymphangiogenesis plays a role. It is an extremely rare cause of osteolysis, so all other differential diagnoses should be considered and ruled out before retaining the diagnosis of disappearing bone disease.
Treatment is fairly disappointing and no single treatment modality has proven effective in actually arresting the disease. Conservative treatment includes ant-resorptive agents (bisphosphonates), immunomodulating substances and radiation therapy, whereas surgical treatment options include resection and reconstruction with bone grafts and/or prostheses versus amputation.
We report on the only two cases that were identified in our database between 1984 and 2008, both affecting the lower limb (one tibia, one femur). In an attempt to limb salvage, these patients initially underwent endoprosthetic replacement of the affected bone segment, but due to disease progression both eventually ended up with a hip disarticulation.
Conclusion: Although benign, this condition can be very aggressive, necessitating amputation to achieve local control.

3.P.10

TWO CASES OF DESMOPLASTIC FIBROMA OF THE SPINE: CASE REPORT AND REVIEW OF THE LITERATURE

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Background: Desmoplastic fibroma (DF) of bone is a very infrequent non-metastasizing osseous tumour with local aggressive appearance. The tendency of local recurrence in published cases is high.
Case reports: We present the clinical and radiological data of a male (35 years) and a female (37years) patient suffering from desmoplastic fibroma. Although in literature spinal lesions are severity rare, in our database two lesions located in the spine (C6 and L4) were identified. The first disturbances have been variable: The lesion in C6 was an accidental finding due to a control examination of a thyroid-ca, whereas the relapse-tumour of the L4 induced lumbago and hypaesthesia of the left heel.
Due to the importance of the thyroid treatment it was decided to control the lesion in C6 in close intervals. The lumbar tumour was initially treated outside and the first relapse was marginal resected at our department 11 years after the first diagnosis. The bone alterations appeared radiographically lytic and cystic.
Discussion: The spine is an unusual location of desmoplastic fibroma which arises in 56% at the long tubular bones followed by the mandible. To our knowledge only a few cases are reported to be located in the spine. DF located spinal, is a very untypical tumour and initial symptoms can be very unequal. Due to this dissimilar symptoms and variable histological appearance the diagnosis can be tricky. At least marginal resection should be achieved because intraleasional resected lesions show a local recurrence of 43%.

3.P.11

BAD PROGNOSIS FACTORS IN RECURRED BONE GIANT CELL TUMORS

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Giant cell tumor (GCT) of bone is an aggressive tumor with high rate of recurrence. Bad prognosis factors were inquired, without a definite identification: type of treatment, soft tissue invasion, high proliferation rate at histology, pathologic fracture.
From January 2000 to February 2008, 38 patients affected by GCT were treated in a regional reference centre, 17 male, mean age 32 (range 16-69, median 29); one patient had 2 localizations (tarsal bone and proximal tibia); 3 were recurrences previously treated in other hospitals. Seven cases were in upper limb, 1 case in the sacrum, 30 in lower limb (20 around the knee); fracture at presentation was present in 6 cases; bone aneurismal cyst (ABC) was associated in 4 cases.
Five cases in stage 3 were treated by bone resection followed in 4 cases by allograft and/or prosthesis (no reconstruction in 1 proximal fibula excision); 33 cases were treated by curettage, local chemical (phenole) and mechanical adjuvants (burring), filling with bone grafts in 13 cases, cement in 8 cases, cement and allografts in subchondral area in 11 cases. The sacral lesion was only curetted.
Seven patients developed a local recurrence, in 2 patients twice, for a total of 9 recurrences (19% of treatments). Recurrences occurred in 2 proximal tibia, in 2 distal femurs, in 1 proximal femur, in 1 distal radius and in 1 proximal fibula. The first treatment was bone grafts in 3 cases (23% of recurrence), bone cement and grafts in 2 cases (18% of recurrence), cement in 1 case (12% of recurrence), resection in the proximal fibula with severe soft tissue invasion. Two patients with associated ABC developed a recurrence and two with fracture at pIn this study, increased rate of recurrences occurred with pathologic fracture at presentation, soft tissue invasion and ABC association.

3.P.12

MORPHOLOGICAL AND IMMUNOPHENOTYPIC FEATURES OF METASTATIC GIANT CELL TUMOURS OF BONE: CLUES TO PATHOGENESIS

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Giant cell tumour of bone (GCTB) is a primary tumour of bone characterised by a proliferation of mononuclear stromal cells and infiltrating macrophages and osteoclast-like giant cells. GCTB has a variable and unpredictable course and can produce metastatic lesions, mostly in the lungs, in up to 3% of cases. Whether these represent tumour implants rather than true neoplastic secondaries is uncertain. In this study, we analysed morphological and immunophenotypic features of primary GCTBs which metastasised to the lung as well as the metastatic lesions themselves in order to determine if these would provide a clue as to the mechanism of lung metastasis in GCTB.
17 cases of primary GCTB which metastasised to the lung and the lung metastases in these cases were obtained from IOR, Bologna. Morphologically, primary tumours showed variable features, often containing both giant cell-rich and mononuclear stromal cell-rich areas. Mononuclear cells showed frequent mitotic activity and a degree of nuclear pleomorphism; none of the tumours showed cytological features of malignancy. The tumours were highly vascular and frequently contained dilated thin-walled blood vessels and large areas of haemorrhage. GCTB lung metastases were generally small and contained osteoclast-like giant cells and mononuclear stromal cells which showed typical mitotic activity; cytologically, the metastatic tumours were relatively bland and showed little nuclear pleomorphism. Expression of HLA-DR (an allele of which has been associated with a more aggressive GCTB phenotype) and smooth muscle actin (SMA) was noted in stromal cells in primary and secondary GCTBs; frequently, the same pattern of SMA expression was seen in both primary and secondary lesions. Osteoclasts were vitronectin receptor+, CD14-,HLA-DR- in both primary and secondary GCTBs.
Our findings indicate that mononuclear stromal cells in lung metastases of GCTB often recapitulate the immunophenotype of the primary tumours from which they derive. Taken with the morphological finding that many primary GCTBs are highly vascular and contain areas of haemorrhage, it is possible that the lung “secondaries” of GCTB more likely represent tumour implants than true neoplastic metastases.

3.P.13

TREATMENT OPTIONS FOR RECURRENT GIANT CELL TUMORS OF BONE

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Although the recurrence rate of giant cell tumors of bone (GCTB) is relatively high exact data on treatment options for the recurrent cases is lacking. The possible surgical procedures range from repeated intralesional curettage to wide resection.
214 patients with histologically certified GCTB have been treated at the authors department from 1980 to 2007. 67 patients with at least one local recurrence were included in this study. The mean follow-up was 77.3 months. The data was evaluated according the re-recurrence rate with regard to the surgical procedure for the recurrence.
The mean time until the first local recurrence was 22.0 months; the mean number of recurrences per patient was 1.4. The recurrence occurred in 69.7 % (46 out of 66 patients) within the first two years. If after intralesional procedures (curettage or intralesional resection) no adjunct was used the re-recurrence rate was 58.8 % (10 out of 17 patients) and decreased to 21.7 % (5 out of 23 patients) if a combination of all adjuncts (PMMA + burring) was used. The likelihood of re-recurrence was reduced by the factor 5.508 which was clearly significant ($p = 0.016$). In case of wide resection no re-recurrence occurred. Seven patients (10.5 %) developed pulmonary metastases. Fourteen patients (20.9 %) finally received an endoprosthesis; 12 due to tumor recurrence, 2 due to secondary arthritis.
Recurrent GCTB can be treated by further curettage with additional burring and cementing with an acceptable re-recurrence rate of 21.7 %. The rate of patients finally needing an endoprosthesis is 20.9 %. Due to the high rate of pulmonary metastases recurrent GCTB may be considered as a severe disease.

3.P.14

INVESTIGATION OF TUMOR MARKERS IN GIANT CELL TUMOR OF BONE

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The giant cell tumor of bone (GCT) is a locally aggressive intraosseous neoplasm, with an uncertain biological behavior, constituted of giant multinuclear cells spread over tumoral tissue with a nucleus presenting the same features of the ovoid and fusiform cells forming its stroma. The local recurrence of GCT is often observed, mainly in the first three years after treatment, giving a rate of recurrence ranging in 20 to 50% of cases. Further aggravating the recurrence is the fact that after the relapse, the patient often also presents metastases in other organs.
The aim of this study was to identify and to characterize differentially expressed genes that can be used in the prognostic, treatment and understanding of this physiopathology. To identify novel genes differentially expressed in GCT, we have applied rapid subtractive hybridization (RaSH). Samples of GCT and normal tissues were obtained at Tumor Bank of Barretos Cancer Hospital. After RNA extraction and cDNA synthesis the samples were submitted to Rapid hybridization Subtraction (RaSH) methodology for subtractive libraries elaboration.
The RaSH subtractive libraries reveals the presence of 619 different clones including both normal and tumor tissues were identified. Of these, 450 in tumor sample and 169 in control tissue. Four biomarkers candidates were selected for validation: ZAK, KTN1, NEB, and ROCK1 genes, whose functions are, related to cell cycle checkpoint, transport of organelles, cytoskeletal matrix and cell adhesions. The validation of selected differentially expressed genes was performed using real time PCR. The putative molecular markers found in this work may help to find the basis for a molecular comprehension of GCT, thus improving diagnosis, treatment and outcome for patients with this tumor.

3.P.15

BROWN TUMOURS OF HYPERPARATHYROIDISM SIMULATING MULTICENTRIC GIANT CELL TUMOURS OF BONE- A CASE REPORT

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Multifocal osteolytic lesions of the skeletal system are a challenge regarding diagnosis especially when multinucleated giant cells which are not specific for a tumour entity are found in the histological specimen. Therefore multiple differential diagnosis have to be considered such as metastases, primary malignant bone tumours, multicentric giant cell tumour of bone and brown tumours of primary hyperparathyroidism.
A 49 year old woman underwent medical investigation in an external surgical department due to right hip pain after a fall. The radiologic skeletal status surprised with multiple osteolytic pelvic lesions and one tumour in the left scapula and first histological diagnosis described a giant cell tumour of bone with malignant aspects. After confirmation of this diagnosis by a second histopathological inquiry accomplished by a bone tumor specialist the patient was transferred to our tumour centre. To exclude the differential diagnosis of brown tumours a close look on the parathormon level was done which revealed an exorbitantly high serum amount of 922.7 pg/ml (normal 15-65 pg/ml). Further examination confirmed a parathyroid adenoma. After its extirpation serum levels of parathormon decreased and two months after therapy with high dose calcium substitution radiologic controls show a decline of osteolysis with bone consolidation.
Brown tumours of hyperparathyroidism have always to be considered as a rare differential diagnosis of multiple giant cell containing tumours. The disease cannot be distinguished by the histological pattern but can very easily be excluded by normal parathormon levels. First step of therapy in brown tumours should be surgical extirpation of parathyroid adenomas or carcinomas followed by an endocrinological regime. Only failure of this treatment requires further surgical stabilisation of the bone lesions.

3.P.16

NEW DIAGNOSTIC POSSIBILITIES IN DIAGNOSIS OF RECURRENT GIANT CELL TUMOUR USING POSITRON EMISSION TOMOGRAPHY

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Following intralesional resection of giant cell tumour local recurrence happens in up to 40% depending on type of treatment. Common plain radiography or Magnetic resonance tomography (MRI) often has the problem not to discriminate between scar and recurrent tumour tissue in the cement-tissue border of lesions treated with cement packing. The value of Positron emission tomography (PET) for diagnosis of tumour and recurrence was investigated in these patients.
In 19 patients with giant cell tumour dynamic PET using F18-Fluordeoxyglucose for estimation of FDG turnover was carried out. PET was performed before surgery and as follow up. In all patients giant cell tumour was treated by curettage followed by burring and cement packing. Giant cell tumour was shown by histology in all patients.
All giant cell tumours showed a specific PET pattern with a very high standard uptake value (SUV) of 4.8 in median. In follow up after surgery this value dropped to 0.3. In one case also pulmonary metastasis could be demonstrated. Recurrence was suspected in the follow up in 5 patients by MRI or plain radiography. In all these patients PET could show an elevated SUV above 4.0. In these 5 patients surgery was performed and recurrence could be proven by histology. In one patient MRI showed signs of recurrence but PET showed a SUV of 1.3. In the revision surgery no tumour could be found. In one patient MRI was negative but PET showed a SUV of 5.2 indicating re-recurrent tumour which could be demonstrated by histology.
We conclude that PET is a very helpful tool not only in the first line diagnosis of giant cell tumour but also in diagnosis of metastatic disease and especially for detection of recurrent tumour.

3.P.17

FUNCTIONAL EVALUATION AFTER EN-BLOC RESECTION OF GIANT CELL TUMOR OF THE DISTAL RADIUS

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Giant cell tumor of the distal radius is associated with a high local recurrence rate. En bloc resection of the distal radius and reconstruction using osteoarticular allograft, curettage with PMMA blomb, and allograft arthrodesis are established methods. The aim of the study was to evaluate the functional outcome of our patients with the DASH-Score and the Mayo Wrist score.
In the last 7 years six patients were treated at our department due to a giant cell tumor of the distal radius. Two patients were primary treated with an en bloc resection. The other four were primary treated with curettage packing of the defect with polymethylmethacrylate. In two of these cases a secondary en bloc resection was performed for local recurrence. For evaluation of function in daily live we used the DASH score and the MAYO wrist score.
The mean bone resection length was 5,25cm (5-6 cm).All four patients treated with en bloc resection (primary or secondary) had no recurrence but in two out of that cases a re-operation was necessary because of non union.
At a mean follow up from 27 months (4-95) there were no recurrences or metastases at all.
The flexion/extension of the wrist in currettaged radius was 60°/80° compared with 38°/68° in reconstructed radius. The pronation/suppination was 90°/90° in the currettaged ones versus 77°/77° in the allograft replaced ones.
The functional outcome evaluated with Mayo Wrist Score and DASH score showed an excellent outcome for both groups (84/7,7 Allograft <-> 85/10 Currettage)
Functional outcome of distal radius resection reconstruction using an allograft is highly satisfactory compared with the literature, however we experienced a high risk for pseudoarthrosis. For prevention of non union simultaneous bone grafting at the index operation could be advisable. Thus allograft reconstruction of the distal radius represents a valuable alternative to arthrodesis.

3.P.18

RISK FACTORS FOR LOCAL RECURRENCE IN GIANT CELL TUMOUR (GCT) OF THE LONG BONE

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Giant cell tumour of bone (GCT) is a primary osteolytic neoplasm, histopathologically characterized by osteoclast-like giant cells and clinically characterized by local bone destruction and high recurrence rates. There is a need to identify risk factors for recurrence. In order to reduce the recurrence rate we initiated an international, multicenter, randomised phase II trial with adjuvant zoledronic acid as compared to standard care for high risk GCT patients.
One hundred and sixteen GCT patients, treated at the LUMC from 1971 to 2006, with a minimal follow-up of a year, were retrospectively analysed for the following risk factors for local recurrence: GCT grade III and tumour involvement into soft tissue caused by ingrowth or fracture. Resection was used as treatment in 21 patients (group A), intralesional surgery with cement or adjuvant in 24 (group B) and intralesional surgery with cementation and adjuvant in 71 patients (group C).
GCT recurred in 5% (1/21) in group A. Risk factors were found in 90% of patients without recurrence (18/20). Group B shows a recurrence of 25% (6/24). Risk factors were found in 83% (5/6) of recurring GCTs, compared with 28% in patients without recurrence. In group C, a recurrence rate of 23% (16/71) was found. Risk factors were present in 94% (15/16) of recurrences, compared to 36% (20/55) in patients without recurrence.
Soft tissue involvement and GCT grade 3 and up are risk factors for recurrence in GCT. Recurrence rates are lowest when resection is used. Risk factors may influence the choice of treatment. High risk patients may benefit from resection or systemic treatment with adjuvant therapy.

3.P.19

THE LEIDEN EXPERIENCE IN GIANT CELL TUMORS OF THE SACRUM: DOES EXTENDED CORTICAL EXCISION REDUCE THE RECURRENCE RATE?

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Giant cell tumors (GCT) of the sacrum have a high recurrence rate, up to 33%. Treatment of Giant Cell Tumors (GCT) of the sacrum has many options. Although curettage is more often performed than partial sacral resection the indications are not well described. Large resection in the sacral area is limited, and adequate local adjuvant therapy potentially damages the nervous system. Therefore the type of surgical treatment of sacral GCT is still under debate.
The purpose of this study was to compare clinical outcome after surgical treatment in GCT of the sacrum using two different surgical techniques: curettage and Extended Cortical Excision (ECE). Pre-operative embolisation was routinely performed, followed by curettage or PSR followed by reconstruction if indicated. Between 1994-2005 11 patients were treated for GCT of the sacrum. Eight were female, 3 men. The median age was 43.5 (14-66) years. The median follow-up period was 60 (6-156) months. Five patients were eventually treated by ECE. The other patients were operated on using different techniques, mainly curettage and/or adjuvant therapy.
Two patients died disease-related 42 and 6 months after primary treatment, both metastasized. All other patients are alive and currently disease-free. Six patients had a recurrence, after 33 (4-140) months. Three patients had a recurrence twice. Three patients received radiotherapy, 1 as palliative treatment and 2 as (adjuvant) therapy for recurrence. No recurrences were seen after ECE compared to 86% (6/7) after curettage only, and 50% (2/4) after curettage with adjuvant therapy.
Extended cortical excision may improve the recurrence rate in sacral GCT.

3.P.20

MALIGNANT GIANT CELL TUMOR OF THE TENDON SHEATH OF THE ANKLE: A CASE REPORT

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Giant cell tumor of the tendon sheath (nodular synovitis) is a benign soft tissue tumor, usually affecting older women, that most often occurs in the interphalangeal joints of the fingers, wrist or knee. Malign giant cell tumor of the tendon sheath is rare.
We present a case of a 56-year-old woman presented with a slow-growing, painless mass on the anteromedial aspect of the ankle 5 year duration. Apparent rapid enlargement of the mass was observed and went under surgery. The resected tumor, measuring 50x21x28 mm.cm, was encapsulated and located on the tibialis anterior tendon sheath of the ankle.
The tumor was intracapsular and its margins was clear. We performed radioterapy. The patient was quite well at the last follow-up 12 months after wide excision. It seems likely that may expect the good outcome, superficial location and the minority of the tumor composed of malignant component. However, long-term follow-up is mandatory, due to the poor prognosis.

3.P.21

PAROSTEAL OSTEOSARCOMA CONCOMITANT WITH DISSEMINATED BREAST CARCINOMA: CLINICAL AND RADIOLOGICAL FINDINGS AND REVIEW OF THE LITERATURE

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Osteosarcoma arising on the periosteal aspect of bone comprises a biologically heterogeneous group of neoplasm. Parosteal osteosarcoma is a low-grade malignant tumour originates at the surface of bone comprising 3-6% of all osteosarcomas and 2% of primary osseous neoplasms. It is most common in young and middle-aged adults and occurs most frequently on the posterior aspect of the distal femur or tibia. The radiologic appearance is often characterized by a large, lobulated, ossific mass in a juxtacortical position. Cortical thickening without aggressive periosteal reaction can be present. Typically the medullary canal is uninvolved. Wide surgical resection and reconstruction is the treatment of choice. The overall prognosis for patients with this lesion depends on the stage of the tumor at presentation. The prognosis for a Parosteal osteosarcoma is generally excellent.
We present an uncommon case of elderly women 70 year-old with a surface osteosarcoma in right femur concomitant with disseminated Breast Carcinoma. The radiological findings showed a juxtacortical mass on the anteromedial aspect of the junction between the mid-third and the distal third of the right femur with areas of new bone formation mimicking Periostal osteosarcoma. We observed a typical Parosteal osteosarcoma when the biopsy was performed. The elected treatment was a wide resection with PTR MUTARS and adjuvant chemotherapy controlling local and systemic In conclusion, due to the treatment for the juxtacortical osteosarcomas varies with the diagnosis, an accurate evaluation and appropriate management must be executed to have the best outcomes.

3.P.22

LOW GRADE CENTRAL OSTEOSARCOMA – DIFFICULT TO DIAGNOSE, EASY TO TREAT!

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Low grade central osteosarcoma is a rare intramedullary bone producing tumour. It accounts for only 1-2% of all osteosarcomas. Due to the indolent nature of low grade central osteosarcoma, achieving a correct and prompt diagnosis is the real challenge both from imaging and histology, particularly as it may resemble a benign condition, i.e. Fibrous Dysplasia.
We have reviewed 15 cases of low grade central osteosarcoma with long term follow-up (2 to 22 years) to identify problems in diagnosis and treatment and to assess outcome.
There were 7 females and 8 males with a mean age of 37 yrs (range 11 to 72 years); 13 cases arose in the lower limb (8 femur, 4 tibia, 1 os calcis), 1 in the pelvis and 1 in the upper limb. The average duration of symptoms prior to presentation was over 2yrs. A primary diagnosis of low grade central osteosarcoma was achieved for only 6 cases (4 open and 2 needle biopsies), in the other 9 the primary diagnoses were GCT, cystic lesion or fibrous lesion (both benign and malignant) and all of them had undergone treatment (usually curettage with or without bone grafting for this). Definitive treatment was with surgery attempting to obtain wide margins. Marginal excision was associated with local recurrence in three cases but there were no local recurrences in patients who had a wide excision, even in those with prior treatment. Only one patient has died following the development of multiple metastases after 9 years. The survival rate is 90% at 15 years.
We present this study to show the difficulties in diagnosing this rare type of osteosarcoma and to highlight the importance of wide surgical margins to obtain local control.

3.P.23

LYTIC LESION IN PELVIS: TUBERCULOSIS OR MALIGNANCY

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Clear-cell sarcoma is a very rare tumor, and is almost always associated with tendons or aponeuroses or is metastatic from other organs. Sporadic cases only have been reported involving primarily the bone or extending from soft tissues to surrounding bones. To our knowledge, the ilium has not been previously reported as the primary site for clear cell sarcoma.
We report a rare case of Primary clear cell sarcoma involving right ilium region in a 18-year-old boy presented with a painful swelling over right ilium and limp on right lower limb of ten month duration. He was initially suspected having tuberculosis based on clinicoradiological evaluation and diagnosis of primry clear cell sarcoma could be established on histopathology. Patient was treated with partial excision of the ilium, the remaining ilium was fused with sacrum. Stabilization was achieved with a cortical autograft harvested from the right fibula and fixation with a titanium plate.
The patient had no local recurrences but the plate holding ilium to sacrum broke and was removed in the subsequent surgery after which he developed Trendelenberg's gait.

3.P.24

DEDIFFERENTIATED ADAMANTINOMA. A CASE REPORT

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Adamantinoma is a primary low-grade, malignant bone tumor that is predominantly located in the mid-portion of the tibia. The aetiology of the tumor is still a matter of debate. Histologically, classic adamantinoma is a biphasic tumor characterized by epithelial and osteofibrous components that may be intermingled with each other in various proportions and differentiating patterns.
We report here a particular morphologic variant of adamantinoma characterised by the loss of classic epithelial differentiation. A 17 year-old teenager presented with a long history of a tumor in the left leg. Explorations revealed an osteolytic lesion of the middle shaft of the left tibia with a huge mass invading soft tissues. An intra medullar bone lesion with benign appearance was observed in the right tibia. CT of the chest revealed lung metastases. Histologically, we observed in the left side a pattern of spinde-celled high grade sarcoma without any evident differentiation. Spindle-shaped tumor cells express cytokeratins and vimentin. Ultrasturctural study showed tonofibrils and desmosomes and was helpful to recognize the epithelial nature of the tumour. The diagnosis of dedifferentiated adamantinoma was retained. In the right tibia biopsy revealed fibrous dysplasia. Amputation above the knee was performed followed by chemotherapy. One year later, the patient is still alive with multiple lung metastases.
In our study, we discussed the clinico-pathologic features of this particular pattern of adamantinoma as well as its association with fiobrous dysplasia in this case. A review of literature was done.

3.P.25

CLEAR CELL MENINGIOMA METASTASIZING TO THE SACRUM. CASE REPORT AND REVIEW OF LITERATURE

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Clear cell meningioma is a rare subtype of meningiomas graded II according to the World Health Organisation classification. In spite of its benign appearance, clear cell meningioma has an aggressive behaviour and it is characterized by its inordinately tendency to metastasize.
The purpose of this study is to discuss the clinico-pathological features of this subtype of meningiomas as well as the metastatic pathways.
We wish to report a rare case of a clear cell meningioma metastasizing to the sacrum 17 years after the removal of the primary tumour. A 26 year-old man was referred to our centre for low back pain related to a lytic lesion of the sacrum. He had a history of a tumour of the forth cervical vertebra that was removed when he was 9 year-old. CT scan revealed an osteolysis of the entire sacrum invading the intrapelvic organs and the sacro-iliac joints. Open biopsy revealed a clear cell meningioma. That was the same pattern of the tumour removed 17 years earlier. Chest CT showed lung metastases. The patient was managed conservatively by palliative radiation therapy. One year later, he experienced improvement of pain and walk. The mass was stable.
Clear ell meningioma is an aggressive tumour with a potential to spread via cerebro-spinal fluid and haematologically. Patients with such a tumour should be closely followed for a long time.

3.P.26

EXTENSIVE OSTEOLYSIS AFTER TOTAL HIP ARTHROPLASTY: TUMOR OR TOMUR SIMULATUNG PROCESS?

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Periprosthetic osteolysis after total joint replacement is a well described complication. This normal slowly increasing process is caused by infection, implant loosening or more special, debris induced. However malignant processes may rarely occur at exact this location too. Based on clinical presentation and imaging it is sometimes difficult to exclude a local malignant process. We report two cases of extensive osteolysis after total hip replacement, including their follow up and a review of the relevant literature.
Two female patients developed massive osteolysis in periprosthetic areas (pelvic area and proximal femur as well as distal femur) after being treated by total hip arthroplasty 14 and 18 years ago. In both cases a tumorous process was suspected after imaging and they were therefore referred to our clinic. In one case a rapidly progressing soft tissue swelling with extensive periarticular osteolysis was considered to be a malignant tumour. After an incisional biopsy, an embolisation had to be performed due to continuous massive bleeding. Histology revealed a superinfected polyethylene disease, treated with a two stage revision surgery. The second patient presented with an impending fracture due an unusual osteolysis at the tip of the stem. Here again polyethylene debris was found at biopsy.
Extensive osteolysis and/or soft tissue swelling caused by polyethylene debris may sometimes be difficult to differ from a tumorous process. As a guideline presented by Min WK. et al in 2008 a reactive bone-destroying process normally proceeds slowly in contrast to a more rapid progression in malignant disease. However, as presented in the first of our cases, exemptions may occur. In these cases a biopsy or at least a frozen section at operation should be obtained in order to exclude a real neoplasm.

3.P.27

OSSEOUS SOLITARY FIBROUS TUMOUR – A REPORT OF TWO CASES

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Primary solitary fibrous tumour (SFT) of bone is extremely rare with few cases reported in the literature. The incidence of the lesion is 0.08% of all primary bone tumours (0.1% of primary malignant bone neoplasms). Previously, such lesions may have been reported as haemangiopericytoma (HP).
Despite being previously considered as separate entities, the two types of tumour (SFT and HP) are now generally accepted as related, sharing similar morphological and immunohistochemical features. Cytogenetic and molecular analysis has, so far, been unable to unite or divide the two. Although frequently having a histologically benign appearance or being labelled as intermediate grade, these tumours may exhibit an unpredictable clinical course and behave in an aggressive manner. We present two cases of osseous solitary fibrous tumour (cellular haemangiopericytoma).
Using the histopathology and bone tumour databases at our institution, we identified two patients (one female aged 21 and one male aged 40) with a histopathological diagnosis of osseous SFT. The site of primary tumour in both patients was the sacrum. In the female patient, the lesion was confined to the sacrum and she underwent curettage. In the male patient, the tumour extended beyond the sacrum to the sacro-iliac joint, ilium and gluteal mass, therefore, total sacrectomy was performed. At presentation neither patient had evidence of metastatic spread.
The female patient was disease free at four years with no evidence of recurrence of metastases. The male patient developed metastases in both lung fields and bone (ribs, vertebrae) three years post-operatively and died four years post-operatively.
Orthopaedic surgeons and histopathologists should remain aware of SFT due to its erratic behaviour and the recent move towards unifying it with HP in a continuous spectrum. We recommend early staging and treatment of these tumours, even for histologically benign/low grade lesions, due to their potentially aggressive behaviour.

3.P.28

GRANULAR CELL TUMOURS: A RARE ENTITY IN THE MUSCULOSKELETAL SYSTEM

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Granular Cell Tumours are rare mesenchymal soft tissue tumours that arise throughout the body and are believed to be of neural origin. They often present as an asymptomatic slow-growing benign solitary lesion but may be multifocal. One to two percent of cases are malignant and can metastasise.
Described series in the literature are sparse. We examined our database and identified eleven cases in ten patients treated surgically and followed-up for a period of over six years (May 2002 to January 2009) in our regional bone and soft tissue tumour centre.
Five tumours were located in the lower limb, four in the upper limb and two in the axial skeleton. Mean patient age was 31.2 years (range 8 to 55 years). Excision was complete in one case, marginal in five cases and intra-lesional in five cases. No specimens showed evidence of malignancy. No patients required post-operative adjuvant treatment. Mean follow-up was 19.3 months (range 1 to 37 months), with no cases of local recurrence. One case was multi-focal.
Histopathological examination revealed the classical features of granular cell tumour in all cases. Typically, tumour cells were diffusely and strongly positive for S100 protein by immunohistochemistry, whereas the other markers tested were negative.
We believe this case series to be the largest of its type in patients presenting to an orthopaedic soft tissue tumour unit. We present our findings and correlate it with findings of other series in the literature.

3.P.29

EXTRAORDINARY, TUMOURSIMULATING EPIMETAPHYSEAL FINDING IN A 4-YEAR OLD BOY – A 5-YEAR RADIOLOGICAL SURVEILLANCE

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Epimetaphyseal lesions may occur within congenital dysplasia or can be linked to metabolic, inflammatory and systemic diseases. They can also be caused by trauma or be due to malign or benign neoplasms.
Our case-report concerns a 4-year old boy who was x-rayed the day after falling from a chair and twisting his right ankle. X-ray showed an epimetaphyseal lesion of about 2 cm in diameter, located eccentrically in the lateral site of the distal tibia. A unilamellar periostal reaction could be detected in the lateral slices. On MRI, the lesion seemed to be of chondromatous origin and showed smooth borders with no evidence of surrounding oedema. The adjacent epiphyseal plate appeared as untypically fragmented. In CT-scans, the ventrolateral cortical bone was partially perforated and the lesion showed a tender sclerotic border. Due to the benign aspect, we agreed upon radiologic controls in order not to harm the epiphyseal plate by biopsy. MRI follow-ups revealed a slight but continuous growth. The lesion assumed an increasingly eccentric, tongue-shaped configuration with simultaneously increasing calcifications and mineralisations. After 5 years of radiological surveillance, the patient showed no evidence of growth-disturbance and did not report pain, but an increasing feeling of pressure when wearing boots.
Traumatic causes as well as metabolic, inflammatory and systemic diseases can, considering the patient's history and clinical status, be put aside. The benign aspect combined with the long-term follow-up rules out malignancies. A chondroid matrix with increasing areas of mineralisation imply the diagnosis of a chondromatous tumour, although radiomorphology does not support this assumption; especially not, if age, clinical presentation, eccentric epimetaphyseal location and the involvement of the epiphyseal plate are taken into account. Among the entities left for differential-diagnosis, a dysplastic process e.g. Dysplasia hemimelica, must be considered, although doubts remain. For confirmation of diagnosis, further radiological and clinical surveillance will be conducted.

3.P.30

BELOW KNEE AMPUTATION THROUGH A JOINT SPARING PROXIMAL TIBIAL ENDOPROSTHESIS USING A CUSTOM MADE END CAP

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This case highlights the close association between osteofibrous dysplasia (OFD) and adamantinoma, drawing attention to the role for more radical treatment options when treating OFD. We discuss the advancements in joint-sparing endoprostheses using bicortical fixation. Finally we describe a unique biomedical design allowing for manufacture of an end cap to allow amputation through a custom made joint-sparing proximal tibial replacement as opposed to an above knee amputation.
A 37 year old presented 7 years ago having sustained a pathological fracture of her tibia. Subsequent biopsy revealed OFD, curettage with bone graft was performed. She later developed recurrence, two percutaneous biopsies confirmed OFD. 6 years following her initial diagnosis she was referred to RNOH with further recurrence, a biopsy at this stage revealed a de-differentiated adamantinoma. A joint-sparing proximal tibial replacement was performed and adjuvant chemotherapy administered, she remained well for one year. Recurrence was noted at the distal bone-prosthesis interface, histology revealed a high grade dedifferentiated osteosarcoma, limb preservation was not deemed possible and an amputation was performed through the prosthesis. The proximal tibial device was uncoupled leaving a residual 7 cms insitu, a small custom made end cap was attached to the remaining prosthesis and a myocutaneous flap fashioned over it, this ultimately enabled the patient to mobilise well with a below–knee orthotic device.
This case highlights the need for more radical surgery when treating cases of OFD and the relationship between OFD and adamantinoma. It also introduces a joint-sparing proximal tibial device for use in proximal tibial tumours that do not invade the proximal tibial metaphysis. The biomechanical design solution has given us the unique option of preserving the knee joint allowing the patient a below knee amputation whereas previously an above knee amputation would have been performed thereby significantly reducing her functional outcome.

3.P.31

BONY HYDATID DISEASE OF SUPERIOR AND INFERIOR PUBIC RAMUS AND RETRORECTAL SPACE: A CASE REPORT

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Echinococcal cysts are mostly found in the liver followed by the lungs, spleen, ovaries, kidneys, brain, bones and heart, but rarely elsewhere in the body. Disease can take place either directly from contact with infected dogs or indirectly from the ingestion of contaminated water or food. Skeletal disease is rare and is usually due to secondary extension after haematogenous spread of the infection.
We present a case of hydatid cyst involving superior and inferior pubic ramus and retrorectal space in a 22 years old male patient, which is not a common site for the occurrence of this disease. Total cystectomy was performed for retrorectal cyst, curettage and bone cementing was done for the bony involvement.
He was well after 1 year follow up. Diagnosis is usually difficult and MRI is a good tool for reaching diagnoses. Curettage and bone cementing can be a treatment option for decreasing bony recurrences.

3.P.32

OSTEOLIPOMA IN PROKSIMAL THIGH: A CASE REPORT

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Although soliter lipomas are very common soft tissue tumors, osteolipomas are rare.
We present a case of a solitary osteolipoma of the inguinal region in a 37 year-old male who was referred for a inguinal mass causing pain and compression of the neurovasculer structures of the inguinal region. The computed tomography scan helped to clinch the diagnosis and histpathology confirmed it. The well- demarcated, firm tumor was excised arising adjacent to the neurovasculer structures of the inguinal region.
Osteolipomas should be kept in mind in the different diagnosis of soft tissue masses as an extremely rare benign lesion.

3.P.33

PRIMARY INTRAVASCULAR LEIOMYOSARCOMA

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Primary vascular leiomyosarcoma is a rare, aggressively malignant connective tissue tumour, which arises from smooth muscle cells of the vessel walls. This neoplasm involves the extremities in about of 30% reported cases. Preoperative angiograms with CT scans and MRI in conjunction with the clinical signs of vascular and biopsy and immunohistochemical studies are useful tools in the diagnostic and operative planning of intravascular leiomyosarcoma.
We report the case of a 34 year-old woman who was referred to us presenting pain, palpable mass in the right inguinal area and tenderness, deep venous thrombosis symptoms and motor dysfunction of her right leg. Biopsy was performed with the diagnosis of Leiomyosarcoma (IIB) of iliac and femoral right veins treated with wide resection and reconstruction of vessels with vascular prosthesis achieving excellent results.
In conclusion, complete surgical resection of the vessel segment is the therapy of choice. Adjuvant therapy, chemotherapy or radiation therapy combined with surgery, is often used for patients with poor prognosis.

3.P.34

SCLEROSING EPITHELOID FIBROSARCOMA OF THE BONE: A CASE REPORT AND SURVEY OF THE LITERATURE

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Sclerosing epitheloid fibrosarcoma (SEF) is an extremely rare soft tissue sarcoma arising from connective tissue cells of mesenchymal origin. SEF mostly occurs in extraosseous sites in the soft tissue; however two cases of primary localization in the bone have been described. Despite benign cytological features the clinical course is complicated by a high local recurrence rate and late metastases. SEF represents a clinically challenging entity especially because no standardized treatment regimens are available.
We report a 16-year old female patient who showed persistent load-dependent pain focused on the right proximal tibia. Radiological evaluation revealed an osteolytic lesion and the diagnosis of a benign bone cyst was consented. The tumor was surgically removed. Only after recurrence of the tumor and repeated histopathological analysis diagnosis of SEF could be established. Because of the bone localization of the tumor the patient underwent standardized neoadjuvant chemotherapy analogous to the European-American EURAMOS-1 protocol for the treatment of osteosarcoma followed by tumor resection and endoprothesis. Histopathological analysis of the resected tumor showed >90% vital tumor cells suggesting no response to the neoadjuvant chemotherapy. Therefore, therapy was reassigned to the CWS protocol of the German Society for Pediatric Oncology and Hematology (GPOH) for treatment of soft tissue sarcoma. To date, the patient is alive and no metastases of the primary tumor can be detected.
SEF represents a taunting clinical entity due to deceptive histopathological features and rare occurrence. Localization in the bone represents an additional challenge with regards to the therapeutical approach. Standardized treatment regimens are currently not available for SEF. This case report, to our knowledge, is the first outlining a therapeutic approach in detail. Our data suggest that SEF may be resistant to a chemotherapy regimen containing Cisplatin, Doxorubicin and Methotrexate despite close association to the bone, possibly indicative of the soft tissue histogenesis of this tumor. The response to the soft tissue sarcoma targeting CWS chemotherapy remains to be determined.

3.P.35

"SPONTANEOUS" REGRESSION OF ADVANCED RETROPERITONEAL LEIOMYOSARCOMA AFTER THE END OF SALVAGE CHEMOTHERAPY

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A case of advanced retroperitoneal leiomyosarcoma is reported in a patient, who experienced a complete regression of her fatal illness.
A 66-year old woman presented with a 1-year history of intermittent lower abdominal pain. An ultrasonogram (USG) and computed tomography (CT-scan) revealed multiple soft tissue masses particularly in the lower retroperitoneal space and also 3 liver nodules. USG-guided biopsy was done and histologically confirmed poorly differentiated leiomyosarcoma. The patient underwent successful macroscopically complete en bloc resection of all tumor masses with the exception of 12 liver metastases which had been resected 6 weeks after the initial surgery. 11 months later USG showed disease progression with diffuse inoperable liver metastases, intraperitoneal and retroperitoneal tumor nodules. We introduced salvage chemotherapy (ChT), using intravenous infusion of ifosfamide 1.8 g/m^2 on days 1-3 with mesna, and intravenous bolus injection of doxorubicin 60 mg/m^2 on day 1. After 4 courses of treatment USG showed partial regression of metastatic disease. When the patient received the 8^{th}, i.e. the last cycle of ChT, USG confirmed further disease regression with only 2 residual metastases in liver. 6 months later USG showed further regression of liver metastases. Another follow-up USG at 9 months and 12 months did not reveal evidence of residual metastases. Almost 2 years after the end of ChT the patient is asymptomatic, well and has no evidence of disease at 41 months after the diagnosis.
The „spontaneous" further regression of metastatic leiomyosarcoma after the end of salvage ChT in our patient would be exceptional phenomena. Although we cannot exclude the remote possibility of "delayed" further response to ChT, generally poor response rate to ChT in leiomyosarcoma would make it very unlikely.

3.P.36

RARE PERIARTICULAR OSSYFYING LIPOMAS MASQUERADING AS MALIGNANT SOFT TISSUE TUMORS

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Ossyfying periarticular lipoma is a very rare entity. Lipomas undergo involutional changes like chondrification, calcification and very rarely ossification. These changes result in altered clinical, radiological and histopathological features leading to diagnostic challenge in differentiation from the soft tissue tumor like synovial sarcoma, liposarcoma and rhabdomyosarcoma.
We present a series of three cases of ossifying lipomas presenting as soft tissue tumor around the knee, shoulder and hip joints. All the tumors revealed calcification and ossification on plain X-rays and on MRI/CT Scans. Clinico-radiological evaluation lead to a similar diagnostic dilemma in our series and a confirmed diagnosis of ossifying lipoma became possible only after histopathology. All the three tumors were excised completely without any recurrence during last 3 1/2 years of follow-up.
We recommend the early imaging by MRI/CT scan with closed core biopsy to exclude the malignant pathology and complete excision of the tumor with early mobilization of the adjacent joint.

3.P.37

RESECTION OF A CHONDROMYXOID SARCOMA FROM THE DORSAL COLUMN – CLINICAL CASE

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Condromixoid sarcoma is a rare tumor (about 2,3% of soft tissue sarcomas in one of the series published) occurring mainly in muscular part of extremities. The reconstruction after block resection of tumor lesions of dorsal column invading the thorax almost always represents a great challenge to the surgical team.The case presented reports an infrequent location of this rare tumor what highlights it in an oncologic point of view. From the surgical point of view the surgical steps of wide tumor resection are described and of the reconstruction of the dorsal column and the involved thoracic region (adjacent to vital structures) what resulted in an asymptomatic correction.
The authors present a case of a 47 years old patient operated to a volumous dorsal condromixoid sarcoma, practically asymptomatic, with invasion and compression of the neurological space and thoracic cavity. After biopsy, a wide resection of the tumor was made, using a double surgical approach (anterior and posterior), with resection of posterior part of vertebras D6-D9 and part of the 7th, 8th and 9th costal arches. The reconstruction consisted in correction of thoracic wall with prosthesis and stabilization of column with pedicular instrumentation from D5 to D11. The post-operatory recover had no complications and in clinically the patient is asymptomatic.
Only the elevated level of suspicion conducted the realization of biopsy in an apparent innocent lesion. The Condromixoid sarcoma occurs rarely in the nervous axis, what created some difficulties in the histological diagnosis. The dimensions of the tumor mass and its localization were object of great discussion and of detailed surgical planning. After a massive surgical resection, the clinical result after 2 years of follow-up is excellent (patient asymptomatic). The almost inevitable oncological decision of surgery in a malignant tumor with medullar cord compression was the only effective way of treatment.

3.P.38

ELASTOFIBROMA DORSI: A CASE SERIES

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Elastofibroma dorsi is a rare, benign, slow-growing 'pseudotumour' classically presenting as an ill defined mass at the inferior pole of the scapula. Typical symptoms include mass, pain, scapular snapping and impingement like features. There is a predilection for females after the fifth decade of life. The aetiology is unclear.
We identified 15 patients (21 tumours) with a diagnosis of elastofibroma. Seven lesions were found on the left side and fourteen on the right; bilateral lesions were found in six patients. The male:female ratio was eight:seven and mean age at presentation was 60.9 years (range 40 - 71). The mean duration of symptoms (most commonly pain, mass and scapular snapping) prior to presentation was 25.8 months. Eighteen tumours were excised with a mean follow-up of 4.2 years (0.25 – 16). Four lesions were diagnosed by combined MRI and CT guided biopsy, the remainder identified using MRI alone. All patients were asked specifically about symptoms, occupation, family history and employment history (including hobbies). Pain was assessed using the Visual Analogue Score (VAS) and functional outcome using the Stanmore Percentage of Normal Shoulder Assessment (SPONSA) Score. Range of forward flexion of the shoulder joint was also assessed.
In the operative group, the mean VAS score improved from 4.6 (0-10) pre-operatively to 2.5 (0-8) post-operatively. Mean SPONSA scores improved from 61.5% (20 – 100) to 81.8% (30 – 100). Mean pre-operative forward flexion was 135 degrees (70 – 180), this improved to 166 degrees (100 – 180) post-operatively. A high number of patients had been involved in occupations involving heavy lifting. MRI had a 100% sensitivity in identifying elastofibroma when correlated with histo-pathological evaluation.
This series demonstrates that elastofibroma may be reliably diagnosed using MRI alone and, in the symptomatic patient, pain and function may be improved through operative excision.

3.P.39

THE CLINICAL SIGNIFICANCE OF THE FUS-CREB3L2 TRANSLOCATION IN LOW-GRADE FIBROMYXOID SARCOMA

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Low-grade fibromyxoid sarcoma (LGFMS) is a rare soft tissue neoplasm most commonly presenting in young to middle-aged adults. LGFMS is an indolent tumour with a deceptively benign histological appearance. Local recurrences are not uncommon and the tumours can metastasise. A particular gene translocation, FUS-CREB3L2, has been shown to occur commonly in cases of LGFMS. The literature suggests that the FUS-CREB3L2 fusion-gene is a specific marker for LGFMS.
We report the cytogenetic analysis of 29 cases of LGFMS, and clinical outcomes of 21 patients treated surgically between 1998 and 2008 at our regional bone and soft-tissue tumour centre. The mean age was 45.4 years. The most common location of tumours in our series was the lower limb. The mean follow-up was 30.1 months (range 0 to 125 months). To date, there have been no cases of local recurrence or metastasis.
Fifteen of our patients (52.2%) were FUS-CREB3L2 translocation-positive. This suggests either that the translocation incidence in our LGFMS series is lower than other studies, or that reverse-transcriptase polymerase chain reaction (PCR) is substantially less sensitive than the literature suggests. The patients in this series testing positive presented at a younger age (38.2 years, compared to 45.6 years), and had larger tumours than their negative counterparts (mean diameter 97.6mm, compared to 65.2mm), although there was no difference in clinical outcome.
We conclude that PCR testing for the FUS-CREB3L2 translocation is a useful tool for confirming the diagnosis of LGFMS, but has no role in predicting short-term clinical outcome. In our experience it is not necessary to perform wide excision, and marginal margins are adequate. Longer-term follow-up is required to elucidate whether the previously reported recurrence and metastasis rates are a true reflection of the nature of this tumour, and may identify differences in the long-term clinical outcome between translocation-positive and negative patients.

3.P.40

TOWARDS GENETIC UNDERSTANDING OF OLLIER DISEASE

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Ollier disease is a rare skeletal disorder. It is characterized by the occurrence of multiple enchondromas with a marked unilateral predominance mainly affecting medulla of the metaphyses and diaphyses of the short and long tubular bones of the limbs, especially the hands and feet. The risk of malignant transformation is suggested to be up to 35%. We hypothesise that Ollier disease is a mosaic condition as it is polyostotic and because of its unilateral predominance. Here we aimed to identify molecular defects in Ollier disease related enchondromas and chondrosarcomas using high resolution single nucleotide polymorphism (SNP) array approach. Affymetrix SNP 6.0 was performed on 67 samples which include 10 blood samples and 3 matched blood-saliva samples as a control; 13 enchondromas and 26 chondrosarcomas of different grades from 30 Ollier patients and normal DNA from 12 Ollier patients for paired comparison.
All samples were divided into three groups: normals, enchondromas and chondrosarcomas. The number of numerical genomic changes in the chromosomes were not different for the enchondromas ($p=0.36$) while large genomic aberrations were seen in chondrosarcomas as compared to normals ($p=0.01$). Copy number variation (CNV) analysis showed 95K amplification at 4q13 in 5 out of 13 enchondromas and a 2K deletion at 14q11 in 6 out of 13 enchondromas. Paired loss of heterozygosity (LOH) analysis failed to show LOH in 5 enchondromas at higher resolution. Paired LOH was observed at 3q, 5p, 6p, 6q, 7q, 9p, 12p, 13p and 13q in 7 high grade chondrosarcomas associated with loss of chromosomes.
The results of this study indicate involvement of chromosomes 4 and 14 for the development of enchondromas. We were unable to detect LOH in enchondromas at 1Mb resolution containing approximately 500 SNP probes. High grade chondrosarcomas showed LOH at different chromosomes. In future, we will study LOH and CNV changes at gene level and select candidate genes.

3.P.41

SHOULDER SYNOVIAL CHONDROMATOSIS WITH COMBINED INTRA AND EXTRA-ARTICULAR INVOLVEMENT - A CASE REPORT.

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Primary synovial chondromatosis, defined by Jaffe (1951), is a rare, benign arthropathy, of unknown aetiology, distinguished by the chondroid metaplasia of the synovial membrane of the joint, bursa or tendon sheath, which leads to the formation of loose bodies, usually intra-articular. It is characteristically monoarticular and the knee, hip and elbow are the joints most commonly affected. The shoulder is a rare localisation and the extra-articular involvement even rarer, with only few cases presented in the literature.
The diagnosis is possibilited by the clinical examination and by the confirmation of the presence of multiple intra-articular loose bodies by roentgenographic studies and magnetic resonance (MR). The treatment is always surgical. Malignant degeneration of synovial chondromatosis into chondrosarcoma is described, although rare. We report an exceptionally rare case of synovial osteochondromatosis of the
shoulder with combined intra and extra-articular involvement in a 28 years old female patient, former athlete. She presented with a five-year history of shoulder pain and slight limitation of motion. Radiographic examination and magnetic resonance imaging led us to the diagnosis of synovial chondromatosis of the shoulder. The patient underwent arthroscopic removal of the intra-articular loose bodies and partial synovectomy. The subscapularis recess was then identified through an anterior deltopectoral incision and multiple loose bodies were removed from within. Primary synovial chondromatosis of the shoulder is rare (5% of the cases) and the involvement of the extra-articular shoulder site is even rarer. Bloom and colleagues reported ten cases involving the shoulder in a meta-analysis of 191 synovial chondromatosis cases.
The arthroscopic removal of the loose bodies combined with the partial sinovectomy has demonstrated efficacy and low recurrence rates, allowing excellent visualization of the joint, decreased morbidity and early functional return. Nevertheless, we think that this approach may become insufficient when the extra-articular involvement is verified.

3.P.42

EFFICACY OF PERCUTANEOUS RADIOFREQUENCY ABLATION FOR THE TREATMENT OF CHONDROBLASTOMA AND CHONDROMYXOID-FIBROMA – PRELIMINARY RESULTS

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Percutaneos radiofrequency (RF) ablation of osteoid osteoma has been proved as an effective treatment. However, there is limited data regarding other tumors. It also has been described in the treatment of other benign and malignant tumors like chondroblastoma and metastasis. In fact, one of the reported cases of chondroblastoma that were treated with RF was radiological small lesion erroneously diagnosed prior to treatment as osteoid osteomas. It was diagnosed as chondroblastoma only retrospectively. The aim of this study is to describe the success of RF as a definitive treatment and as an alternative to traditional surgery for the treatment of large chondroblastoma and chondromyxoid-fibroma which were diagnosed as such prior to ablation. From April 2006 to April 2007, 3 patients with chondroblastoma and 1 patient with chondromyxoid-fibroma were treated with RF ablation using cool-tip probe. Three procedures were done in the CT suit and one in the operating room. There were 3 girls and 1 boy. Mean age was 12 y 9 m (range 11 y 6 m -14 y 6 m). Clinical and radiological follow-up was performed to assess outcome. The mean follow-up was 23.25 months (range 20-3Three patients healed after single treatment and one needed repeated treatment. No immediate or delayed complications were observed. Follow up MRI showed no enhancement in the lesion and an extra-lesional sclerotic ream signifying RF effect beyond the lesion area. All patients returned to complete normal painless function.
In spite of the small number of patients, percutaneous RF ablation was shown to be an effective and safe minimally invasive procedure for the treatment of chondroblastoma and chondromyxoid-fibroma, avoiding the morbidity of commonly used wide excision surgeries.

3.P.43

AN ASSOCIATION BETWEEN BREAST CANCER AND CHONDROSARCOMA

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Within a study group of 102 consecutive patients diagnosed at a supra-regional bone tumour unit with chondrosarcoma of the femur, tibia or humerus, an association with previously treated breast cancer was noted.
There were 58 female patients and 44 male patients. The study group contained six females (10%, mean age 53 years) who had previously been treated for breast cancer, a higher proportion than would be expected. They were referred following identification of a solitary area of increased activity on routine screening with isotope bone scan, presumed to be a solitary bony metastasis.
Most (86%) of this breast carcinoma sub-group had developed low-grade bone chondrosarcoma (Trojani grade 0.5-I) and only one case (14%) had developed high-grade chondrosarcoma (Trojani grade II-III).
A suspicious long bone lesion on bone scan in a patient with a past medical history of breast cancer must, therefore, not be assumed to be a metastasis without further investigation; the possibility of a chondral lesion should be considered. It is important that patients receive a full multidisciplinary team investigation prior to treatment in order to obtain the correct tissue diagnosis, as the management of these conditions is often different.
Our study suggests there may be a relationship between patients previously treated for breast cancer and the development of subsequent chondrosarcoma.

3.P.44

ADJUVANT RADIOTHERAPY IN SACROCOCCYGEAL CHORDOMA SURGERY: A NECESSITY?

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Sacrococcygeal chordoma is a slow growing, malignant tumour with a clinical poor outcome due to a high local recurrence (LR) rate. Several studies emphasize that margin-free tumour resection is the most important predictor of survival and LR in patients with sacrococcygeal chordoma. However, a high recurrence rate still remains. The purpose of this report is to define the role of postoperative radiotherapy (RT).
15 patients (7 females and 8 males) underwent surgical treatment for sacrococcygeal chordoma between 1981 and 2003. The mean age at surgery was 54 (range 31-70) years. The mean follow up was 8.5 (range 4 – 20) years. Most patients suffered from local swelling and pain; only one patient had a mild urinary continence being the only pre- and postoperative neurological deficit. Mean time of preoperative complaints was 4.5 (range 0.8 – 8) years. In 9 patients an en bloc resection was performed, in 6 patients a subtotal resection was achieved. Most patients with a subtotal resection received RT (5/6 patients) following surgery, patients with en bloc resection only received RT (> 50Gray) after LR (6/9 patients).
After en bloc resection (no initial RT) all patients had local recurrence of the tumour with a mean time to recurrence of 3 (range 0.8 – 13) yrs. Only two patients in the group with subtotal resection had LR after 11 yrs. Six of 9 patients with LR after en bloc surgery received RT after recurrence and had a survival of at least 9 (range 5 – 20) years. There were no major complications. The time to recurrence was significantly longer in the group that received immediate RT after surgery, even after resection with irradical margins. There was no difference in survival between both surgical groups.
Our results suggest that postoperative RT is more important in the prevention of local recurrence than margin-free tumour resection. This supports the strategy to add radiotherapy as a standard adjuvant therapy to tumour resection in patients with sacrococcygeal chordoma.

3.P.45

SURVIVIN, DR4 AND DR5: POTENTIAL TARGETS IN FUTURE THERAPY STRATEGIES FOR CHORDOMAS?

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Chordomas are rare neoplasms originating from notochordal remnants. They usually affect the midline and the standard treatment consists of surgery and radiotherapy. The present study investigates the expression of survivin, DR4 and DR5 to evaluate potential molecular targets for future therapy-strategies.
The study-group included 33 chordomas obtained from 21 male and 9 female patients. At time of diagnosis the patients' age ranged from 24 to 80 years (51.9 ys.). Tumours were located on the scull-base, in the sacral/coccygeal area and the column in 13, 10, and 7 cases, respectively. Tumour-volume, known in 16 cases, ranged from 3.6 to 668.2 cm^3 (mean size 130.7cm^3). Immunohistochemistry was performed with antibodies against survivin, DR4, DR5. The staining pattern (cytoplasmic and / or nuclear), percentage of positive tumour-cells and staining-intensity were evaluated.
Histologically the tumours were classified as classic, chondroid and dedifferentiated chordomas in 27, 2 and 1 case, respectively. Survivin expression was obtained in 87.5% of the cases. The staining pattern was cytoplasmic in all cases and an additional nuclear staining was detected in two. Staining-intensity was predominantly weak. In 87.9% of cases DR4 staining was investigated in more than 10% of the tumour-cells. The immunoreaction was cytoplasmic (87.9%) and a nuclear staining was additionally detected in two cases. The staining-intensity was predominantly weak. In 81.8% of the chordomas DR5 staining was obtained in more than 10% of the tumour-cells. The staining pattern was cytoplasmic (84.4%) and in one case cytoplasmic and nuclear. The staining-intensity was predominantly moderate.
We hypothesise, based on the availability of new chemo- or immunotherapeutic agents like Mapatumumab (agonistic human monoclonal antibody to DR4, tested in solid tumours) and YM155 (new small-molecular inhibitor of survivin, tested in solid tumours and lymphoma), that survivin, DR4 and DR5 may act as potential molecular targets in future therapy of chordomas.

3.P.46

HMW-MAA AND B7H3 EXPRESSION IN HUMAN CHORDOMA

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Chordoma is the second most common primary malignant tumor of the spine. These tumors rarely metastasize but are considered malignant and, when present in younger individuals, can be aggressive. In the setting of unresectable primary, recurrent, or metastatic tumors the current armamentarium of adjuvant therapy for this condition is very limited. Recent research, however, has identified potential targets for immunotherapy, including the tumor associate antigens High Molecular Weight Melanoma Associated Antigen (HMW-MAA) and B7H3.

The goal of this investigation was to correlate expression of B7H3 and HMW-MAA in chordoma tumors with disease severity and clinical outcome.

Tissue MicroArrays (TMA) were constructed using an automated arrayer to include 70 conventional chordoma tumors obtained from archives at our institution. Triplicate cores (0.6 mm in diameter) from each sample were created and two sets of cores were created for each chordoma specimen. One triplicate sample was incubated in a closed humid chamber with a pool of HMW-MAA-specific mAb, while the other was incubated with mAb specific for B7H3. Samples were washed in PBS and incubated with a secondary antibody for one hour. Staining was evaluated independently by two researchers and scored using validated systems. A retrospective chart review was performed for each chordoma specimen to determine demographic data, disease course, disease status at final follow-up and mortality. Clinical outcomes were then correlated to the expression of HMW-MAA and B7H3 within the chordoma lesions. Kaplan-Meier curves and Cox proportional hazard regression analysis were utilized to facilitate comparisons.

Chordoma tumors from 70 patients were included in this study. Average age at the time of presentation was 57.4 years (31-88 years). Average follow-up was 5.5 years (3.6 months-21 years). Forty-three patients developed recurrences and 10 had metastatic disease. Twenty-three patients (33%) had died of disease at the time of final follow-up. Ninety-seven percent of chordoma tumors stained positive for B7H3 while 44% stained positive for HMW-MAA. No correlation could be drawn between clinical course, recurrence rate, or mortality and tumor expression of B7H3 and HMW-MAA. Kaplan-Meier analysis did demonstrate a shorter survival time for patients whose tumors stained positive for HMW-MAA compared to those whose tumors were negative for the antigen.

The goal of this investigation was to correlate expression of B7H3 and HMW-MAA in chordoma tumors with disease severity and clinical outcome. Results indicate that expression of HMW-MAA may be predictive of more aggressive disease and shorter survival. HMW-MAA and especially B7H3, in light of its near universal expression in the chordoma tumors studied here, may serve as potential targets for adjuvant immunotherapy.

3.P.47

FIBROUS DYSPLASIA AND PAIN: INDICATION FOR TREATMENT?

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Although fibrous dysplasia is a benign bone disease, in few cases patient are suffering from severe pain of the skeletal system. The aim of this study was to evaluate the current state regarding pain of patients with fibrous dysplasia treated at our hospital.
We searched our digital database since 1990 for patients with fibrous dysplasia. Subsequent we verified the histological diagnosis by reviewing the final pathologic report. Additional we called the identified patients by phone to make an enquiry about their pain course and associated treatment. For rating pain intensity we used a numeric rating scale with a range within zero to ten.
We identified 43 patients (21 male, 22 female) with an average age at initial diagnosis of 40 years (range 10 to 72years). The mean follow up was 6 years (range 1 to 23 years). Among these 43 patients we were able to contact 33 by phone. Initial diagnosis was made due to pain in 23 cases, nearly coequal by coincidental examination in 20 cases, for fracture in two cases and for local swelling and bone deformity each time in two cases. Thirty-six patients revealed monostotic and seven patients polyostotic involvement. The following locations were found: three times craniofacial, four times within the spine, eight times at the upper extremity, ten times in the pelvis and 31 times at the lower limb. Two patients were suffering additionally from Mazabraud Syndrome. Actual values at the numeric rating scale regarding pain ranged from 0 to 9 with a mean value of 1. Specific in the polyostotic group we found an average value of 3 and three of seven patients stated a value greater than 5 for persistent pain. Five patients with polyostotic involvement were treated with bisphosphonat for pain control with good response.
It is remarkable that patients with polyostotic involvement have marked higher values for pain intensity at the numeric rating scale. So therefore we should have a closer look for potential reasons explaining that fact. In accordance with previous published studies we found that pain decreased by intermittent intravenous application of bisphosphonates.

3.P.48

THE FROZEN SCAPULOTHORACIC SPACE. A PATHOGNOMONIC SYMPTOM OF PERI SCAPULAR FIBROMATOSIS

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The stiffness of the shoulder can result of many illness. Nevertheless, we observed a severe stiffness of the scapulo thoracic space only in fibromatosis. To precise the real diagnostic value of this symptom, we examined patients with different diseases of shoulder (tumoral and non tumoral).
The passive mobility of the shoulder of 11 patients with peri-scapular fibromatosis was compared to the mobility of those in 50 patients with non tumoral diseases of shoulder (arthritis and rotator cuff pathology), 50 peri-scapular soft tissues tumours, and 100 patients with primitive or secondary malignancies of humerus or scapula.
Results: in 10 of 11 patients with peri-scapular fibromatosis, the passive mobility of the scapulo thoracic space was severely impaired (less than 20°). In non tumoral pathology of shoulder, the passive mobility of the shoulder is frequently impaired but the stiffness hangs only on scapulo humeral articulation. In metastases, sarcoma and soft tissue tumour (except fibromatosis) the passive mobility of the scapulo-humeral joint is usually preserved and the mobility of the scapulothoracic space is always normal even in very huge tumours.
After treatment of fibromatosis, 9/11 patients are in complete remission and the mobility of their scapulo thoracic space restored . 2 patients are in stable disease and one suffers of a residual stiffness of the scapulo-thoracic space.
We conclude that the frozen scapulo thoracic is a specific symptom of peri scapulo thoracic fibromatosis. The restoration of the mobility of the scapulo thoracic after cure of the desmoid tumour confirms its specific role and represents a good marker of the tumoral evolution.

3.P.49

PROGNOSIS AND TREATMENT OF PERISCAPULAR FIBROMATOSIS

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Desmoid tumour is an histological benign tumour. Nevertheless, peri-scapular relapses can decrease the function and intra thoracic progression threaten life. To prevent these complications, damaging treatment (radiotherapy, amputation) are sometimes proposed. To precise the optimal indications of treatment, we reviewed our cases.
Patients: from 1984 to 2008, we treated 11 patients with peri-scapula fibromatosis (mean age 42 (13-58)).Only 4 patients were seen at first hand, 7 for relapses (3 of them after radiotherapy). Treatment was adapted to each patient, in function of age, history of illness, and risks of spontaneous evolution. En bloc extratumoral resection was performed each time, when it didn't expose to heavy functional risk (8). The other patients were treated by contaminated resection, but never invaliding. 4 patients received pre or/and post-operative chemotherapy. 1 received Interferon alpha, and 7 tamoxifen.
Results: with a median follow-up 15 years 3 months, 7 patients suffered of recurrence. No patient died from disease (thoracic complications) or therapeutic complication.. 9 patients are in complete remission and 2 in stable disease.,. Following radiotherapy, local relapses (7 cases) and repeated surgery, functional sequellaes are numerous : 2 circumflex nerve palsies, 3 articular stiffness. Major functional sequellaes came from radiotherapy (limb discrepancy, lung and thorax deformity, skin and muscle atrophy .
Conclusion: in this non predictable illness, therapeutic indications should individually balance risks of spontaneous evolution and of complications of treatment. Besides surgery, needed in fast all cases, but often insufficient, it must be considered the value of interferon, tamoxifen and /or chemotherapy. The most important concept is the necessity to treatment avoiding late sequellaes and particularly radiotherapy or mutilating surgery.

3.P.50

MULTIMODAL THERAPY IN PATIENTS WITH DESMOID TUMOURS OF THE EXTREMITIES

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Desmoid tumors are rare benign but aggressive lesions. They are characterized by bland-appearing fibroblasts, indistinct margins, and the ability of local invasion and recurrence. Though they are not cancer they may metastasize and can cause significant morbidity. Treatment is primarily surgical, although radiation or systemic therapy can be beneficial if surgery is not feasible. We retrospectively reviewed our patients since 1980 in respect to treatment modalities and outcome.
Between 1980 and 2008 26 patients (16 m, 10 f) with desmoid tumours had been surgically treated. The mean age with diagnosis was 37 years (7 – 69 years). The mean age at surgery was 46 years (10 – 81 years). 17 of the patients had only one resection. In 6 patients two resections, in 2 three resections and in one patient four resections had to be performed. Only 7 patients achieved a R0-situation. In 9 patients adjuvant radiotherapy was used. Two patients had several courses of Vinblastine or MTX based chemotherapy, three patients had Sulindac or Tamoxifen, several other patients combinations of different NSARs. All patients were still alive, one patient developed metastatic disease from the initial lesion in the groin to the foot. After an average of 17 months (7 – 42 months) 11 patients showed recurrent disease. 13 patients are without recurrence after an average of more than 9 years. In 4 patient stable disease is seen without progression in 42 to 156 months (Ø 95 months).
In conclusion desmoid tumours did show an inpredictable course of disease. Due to many alterations in treatment in the 28 years since the first patient of this study and the rareness of this disease no clear predicitve factor could be established. Remarkably no patient did need an amputation. A more detailed analysis regarding the dose effect of irradiated patients is intented.

4.O.01

BONE AND SOFT TISSUE SARCOMAS: A CHALLENGE TO THE MEASUREMENT OF PATIENT-REPORTED OUTCOMES

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Disease-free survival and local relapse rates in patients with malignant bone tumors are similar following limb salvage and amputation. However, while there has been considerable interest in comparative function after surgery, as assessed by clinicians, there is less information on patient-reported outcomes (PROs). Interest in PROs has evolved from recognizing the usefulness of measures of (health-related) quality of life (HRQL) and the acceptance that the "gold standard" in such assessments is provided by the individual reporting on his/her own health status.
In the context of cancer and cancer-treatment, the importance of PROs is firmly embedded in the conduct of clinical trials, as documented by the Cancer Outcomes Working Group of the National Cancer Institute (NCI) in the USA. The NCI has promoted the development of appropriate instruments for eliciting and evaluating PROs through the Patient Reported Outcomes Measurement Information System (PROMIS). Similar initiatives have been undertaken in Canada, the United Kingdom, Western Europe and elsewhere. This topic was the subject of a series of reviews in a recent issue of the Journal of Clinical Oncology.
Large studies in the United States and Canada revealed that, among survivors of cancer in childhood and adolescence, those who had had brain or bone tumors experienced the greatest compromise in physical performance, psychosocial outcomes anInclusion of PROs and measures of HRQL are still not routine in the design and conduct of clinical trials, and these are seldom used in regular day-to-day practice by clinical oncologists who have yet to be sufficiently persuaded of the added value provided by such determinations.
However, the orthopedic community lead the way more than 25 years ago with an assessment of HRQL following treatment of sarcomas of the extremities (at that time refuting the commonly held belief that any therapy, no matter how "aggressive", was better than limb amputation). That study enrolled only a small number of patients and the therapeutic (especially surgical) options have changed substantially in a generation, but a "marker" was established and the challenge to provide current evidence remains.
Measures of HRQL that focus on orthopedic problems have been developed and subjected to recent rigorous review. But assessments are subject to many confounding factors such as age, gender, diagnostic details (tumor type, size and location), prior (neo-adjuvant) and subsequent therapy, the era of treatment and the time elapsed since surgical intervention. Sample sizes will need to be very large to address these variables.
Despite the almost consistent problem of small samples, some common findings emerge. Females experience poorer outcomes than males; there can be improvement over time; and, insofar as they are comparable (candidates for amputation are seldom candidates for limb salvage surgery), the differences in HRQL among amputees, patients who had rotationplasties, and those who underwent limb salvage (with endoprostheses or bone grafts) are small.
Measures of functional outcome and HRQL are neither fully inter-changeable nor mutually exclusive, and much remains to be learned from the measurement of PROs in patients with bone and soft tissue sarcomas.

4.O.02

LONG TERM RESULTS IN KNEE RECONSTRUCTIONS WITH MODULAR UNCEMENTED PROSTHESES FIXED HINGE AFTER RESECTION OF BONE TUMORS: A COMPARISON OF TWO CONSECUTIVE DESIGNS OF THE SAME SYSTEM

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Between 1983 and 2006 at Rizzoli 669 knee modular uncemented prostheses were implanted after resection of the distal femur, total femur or proximal tibia. These prostheses include 126 KMFTR prostheses and 543 second generation HMRS prostheses. Patients were followed periodically in the clinic. Data was obtained from clinical charts and imaging studies with special attention to major complications requiring revision surgery. Revision for polyethylene wear was considered a minor complication, since it did not imply failure of the implant. Functional results were assessed according to the MSTS system. Since data could be misleading due to deaths in an oncologic population (although 2/3 of patients were cured or long survivors), to censore the implant unrelated events Kaplan-Meyer curves of implant survival were studied.
In 126 KMFTR group infection rated 13.5%, stem breakage 13%, aseptic loosening 9.5%; change of polyethylene rated 44%. In 543 HMRS prostheses infection rated 8.6%, stem breakage 3%, aseptic loosening 4.8%; revision for polyethylene wear rated 9.6%. Techniques of revisions and their outcome analysed showed about 2/3 of good results, but increased risk of further complications in revised implants. Functional results (MSTS system) were good or excellent in 80% of KMFTR prostheses and in 90% of HMRS.
Decrease of major complications in newer prosthetic design was statistically significant and possibly due to newer materials and modified stem design. Polyethylene wear also decreased significantly. Function was satisfactory in most patients without complications for both groups. Revision surgery is technically demanding and appropriate timing of revision is crucial, since early treatment can improve final outcome.

4.O.03

LONG-TERM COMPLICATIONS IN PATIENTS TREATED WITH ENDOPROSTHESIS OF LOWER LIMB FOR MALIGNANT BONE TUMORS

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Limb salvage has become the most important treatment for patients with malignant bone tumors of the lower limb. Reconstruction with endoprosthesis of the proximal femur and distal femur and proximal tibia is now the most common solution. The data of 180 consecutive patients with malignant bone tumors of the lower limb treated between 4/1987 and 11/1998 were reviewed. The average follow up is of four years.
129 patients had surgery for primary bone sarcoma, six for aggressive GCT and 45 for metastatic carcinoma. 63 patients were reoperated for different complications. The main complications were: local recurrences in 10 patients, infection in 12 patients and mechanical complications in 35 patients. 28 patients were operated two times and 24 patients more than two times.
14 patients have undergone amputation: six because of local recurrences, four because of infection, and two for post-surgical ischemia.
Eight of the 12 infections occurred after a re-operation.
35 patients had mechanical complications: 14 patients were reoperated to replace the polyethylene bushings in of the first model of HMRTS prosthesis (Howmedica), five patients had ruptures of the femoral stem, three patients suffered mobilization of the tibial stem and two of the femoral stem, six patients required a patella prostheses for local pain.
Two patients had acetabulum wear and three had hip dislocation.
In our experience endoprosthesis reconstruction after resection of bone tumors of the lower limb is a feasible procedure for limb salvage. We must consider that more than 30% of these patients will be re-operated for different complications and that 50% of infections occours after a new surgical procedure.

4.O.04

INSTABILTY OF THE ENDOPROSTHESIS IN BONE TUMORS. A RETROSPECTIVE ANALYSIS

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The aim of this study was to analyze the frequency and reveal the most common reasons of the endoprosthetic instability in patients with malignant bone tumors. From 1992 - 2008, 625/515 patients, endoprosthetic replacement of major joints were performed. The median age of the patients was 30.3 years (13 to 72 years).
Aseptic instability was observed after 3/71(4.2%) humeral joint replacement out of total operations at this location, after 4/80 (5%) hip prosthesis, after 19/133 (14%) proximal tibial prostheses, after 44/299 (14.7%) distal femoral prostheses and after 2/37 (5.4%) total femur replacements.
The retrospective analyses has shown that the reasons of instability were the following: aseptic loosening of the stems of endoprosthesis in 26 cases (24.4%), stem break in 31 (36.1%), endoprosthetic unit destruction in 10 (11.6%), untwistment of fixational screws in 10 (11,6%), migration of hip endoprosthesis components in 2 (2.3%) and endoprosthesis dislocation in 12 (14%). The timing of endoprosthetic instability ranged from 7 days to 12.2 years (average 26.2 months). Statistic analyses was performed in a group of patients with aseptic endoprosthesis instability developed after proximal tibia and distal femur resection.
We conclude that the most frequent reason of aseptic instability was endoprosthetic stem break. The instability rate was actually lower among the patients who had underwent 5-10cm distal tibia resection comparing with the group of 10-15cm bone mass resection ($p=0.05$). Femoral resection enhanced the instability frequency comparing with proximal tibia resection in the group of 5-10cm bone mass resection ($p=0.05$).

4.O.05

OSTEOARTICULAR ALLOGRAFT RECONSTRUCTION AFTER DISTAL RADIAL RESECTION FOR BONE TUMORS: A SERIES OF 18 CASES AT 1.5 TO 8 YEARS FOLLOW-UP

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Different techniques were proposed for reconstruction after distal radial resection for bone tumors. When not dealing with heavy workers or complex revision cases, a motility preserving procedure can be used. From 1999 to 2007 we performed a reconstruction with an osteartícular allograft in 18 patients.
Age of the patients ranged from 13 to 56 years. Histotypes were: giant cell tumor in 16 patients, Ewing sarcoma in 1, osteosarcoma in 1. Neadjuvant chemotherapy was used in Ewing and osteosarcoma patients. Length of resection ranged from 5 to 13 cm. An accurate host-graft capsulorraphy was performed to reestablish joint stability; no adjunctive distal radioulnar stabilization procedures were used. In one case the procedure was performed after a failed previous graft-arthrodesis; in this case also a proximal row carpectomy was performed.
Non-union of the allograft occurred in 2 cases. In one case autologous cancellous bone grafting from the iliac crest was performed. In the second case the patient due to mild symptoms has till now refused further surgery.
No septic complications occurred.
One patient presented a fracture of the allograft; a revision procedure was performed with a new allograft but also the second graft failed and an arthrodesis was performed. This was the only complete failure of our series.
Follow-up ranged from 20 to 103 months. No recurrences (local or distant) were observed. The patients were evaluated with radiographic and clinical examination. Functional evaluation was performed using ISOLS-MSTS score, a wrist-specific functional score (PRWE) and a comprehensive evaluation of upper arm function score (DASH).
The oncological and functional results in our series highlight that a functional wrist can be restored with an osteoarticular allograft after distal radial resection for bone tumors. Deterioration of the results could occur in the long-term and thus further monitoring with a longer follow-up is needed.

4.O.06

EXTRA-ARTICULAR BONE- OR SOFT TISSUE TUMOUR RESECTION OF THE KNEE JOINT; RESULTS IN 34 PATIENTS

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Limb-sparing surgery has become the preferred surgical treatment of malignant bone tumours of the knee. In patients with intra-articular extension of their tumour, extra-articular limb sparing surgery can prevent the knee from amputation. In a retrospective study between January 1985 and December 2007, we performed 34 extra-articular tumour resections of the knee-joint for a bone- or soft tissue tumour in the distal femur or proximal tibia with (suspect) intra-articular tumour extension into the knee on MRI. Contra-indications were extension of the tumour into the extensor mechanism and/or tumour involvement of the neurovascular bundle. Osteosarcoma (23/34) was the most common primary malignancy. Mean age was 36 years (17-70) and the mean follow up was 9 years (1-19).
Patient survival rates at 5 years and 10 years are 78% and 58% respectively, mean patient survival was 47 months (8-211). In 12 (35%) patients, the primary implanted prosthesis failed during follow up. Prosthetic survival rates including minor revision surgery were 63% at 5 years and 36% at 10 years. Six (18%) patients had local recurrence of their malignancy, 5 of them in the popliteal fossa. Local recurrence was significantly correlated with marginal margins ($P<0.05$). Fifteen patients had major complications (44%) mainly deep infection in proximal tibia resections and aseptic loosening in distal femur resections. Aseptic loosening was significantly correlated with non HA-coated stems ($P<0.05$). Functional outcome scores according to MSTS (mean 81, (65-93)) and TESS (mean 85, (56-98)) of survivors are good.
Our results suggest that extra-articular tumour resections of the knee-joint can provide a functional endoprosthesis and can be an alternative for primary amputation. However it is a technical demanding procedure with acceptable local recurrence and high complication rates in patients with, in general, poor survival.

4.O.07

TREATMENT AND OUTCOME OF PAROSTEAL OSTEOSARCOMA – BIOLOGICAL VERSUS ENDOPROSTHETIC RECONSTRUCTION

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Parosteal osteosarcoma is an uncommon tumour. Different methods of surgical treatment have been reported. Aim of this study was to investigate differences in outcome after biological and prosthetic reconstruction.
Since August 1969, 28 patients have been treated at our institution. Average age was 26 years, range 15 to 59 years. Patient data was retrospectively reviewed within the prospective database of the *Vienna Tumour Registry*. Average follow-up was 133.9 months, range 8.4 to 382.6 months. Two patients died of disease 8.4 and 81.4 months after operation, respectively, another patient died due to unrelated causes 330.4 months postoperatively. All surviving patients were followed for a minimum of 3.6 months.
Location of the lesion was the distal femur (19), proximal humerus (four), proximal tibia (three), mid-diaphyseal and proximal femur (one each). In 12 patients endoprosthetic reconstruction was indicated. Biological reconstruction was performed in 11 patients. Three patients underwent rotationplasty, two patients were amputated. Eight of 12 patients with endoprostheses have been revised, five have had multiple revisions. Causes for revision were bushing wear (four), aseptic loosening (four), infection (three) and periprosthetic fracture (one). There was no local recurrence in the endoprosthetic group. Two of 11 patients with biological reconstruction underwent revision due to pseudarthrosis and femoral fracture, respectively. There were two cases of local recurrence requiring secondary amputation. Two patients with rotationplasty underwent revision for wound healing disturbance and thrombectomy, respectively. Three patients developed lung metastases, leading to death of disease in two cases of amputation and rotationplasty.
One patient with endoprosthetic reconstruction was alive 129.0 months after pulmonary metastasectomy. Functional outcome was satisfactory in all patients; there were no significant differences between patients with endoprosthetic or biological reconstruction.
Biological reconstruction showed less revisions compared to endoprostheses, however, exact preoperative planning is required to obtain clear margins of resection.

4.O.08

LATE SIDE EFFECTS OF NEOADJUVANT CHEMOTHERAPY AND RADIOTHERAPY IN PATIENTS WITH LOCALIZED EWING' SARCOMA

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Prolonged survival have been reached in the last two decades in patients with Ewing's sarcoma due to combination of chemotherapy and radiotherapy.
We report the analysis of 493 patients treated according to 4 different protocols in 23 years (Jan1983- Dec 2006).Aim of this study was to evaluate the occurrence of late toxicities as Second Malignant Neoplasms (SMN), Cardiomyopathies and sterility,
Methods:We reviewed our database to find out all those patients aged from 1 to 40 yrs with localized Ewing's sarcoma who were treated with chemotherapy according to 4 different protocols from 1983 to December 2006. Data were updated at Dec 2008
Results: 493 patients had adequate follow up and meet the eligibility criteria. Median age was 16 yrs (1-40) female/male: 183 / 310 .Median overall survival 69 ms (4-302).220 patients died and 273 are alive. 44 pts received HDCT + PBSCR. Eleven SMN were found : 2 AMLeukemia, 2 parotid adenocarcinoma, 1 melanoma, 1 thyroid cancer and 5 radioinduced osteosarcoma . The interval between Ewing's sarcoma diagnosis and leukaemia diagnosis was shorter then interval between Ewing's sarcoma and RT osteosarcoma. Six patients reported a Cardiomyopathy : in 4 cases it was mild and pts are well compensated ,2 patients needed heart transplant,.One of these two pts received also a kidney transplant due to chronic renal failure due to previous chemotherapy. Fertility: 17 women became pregnant after chemotherapy, 20 women experienced postTx amenorrea: 7 pts received RT in pelvic area , 9 did HDCT, 3 pts were over 30 yrs old. 9 male became father. 8 male patients did sperm analysis 3 azospermia , 4 oligospermia and 1 normal sperm count.No congenital abnormalities in offsprings were reported.
Conclusions: In this casuistic the Cumulative Risk to have a SMN at 5 yrs is 1.8% and 2.9% at 10 yr. The SMN cumulative incidence in Ewing's sarcoma seems to be lower then in our previous casistic in osteosarcoma patients (ASCO 2006).

4.P.01

PARTIAL EXCHANGE OF KMFTR PROSTHESES TO MUTARS AS A TREATMENT OPTION FOR STEM FRACTURES IN LONG-TERM SURVIVORS

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A revision of a first generation KMFTR prosthesis due to stem breakage is a problem oncologic surgeons are regularly faced with. We designed an adapter which allows us to connect new MUTARS components to the original KMFTR devices. Thus it is possible to bypass an exchange of the whole prosthesis.
We used this adapter in 10 patients. Time of revision was in average 16.6 years after primary implantation of the KMFTR prostheses. Reasons for revision were femoral stem breakage (n = 5), breakage of the tibial component (n = 3) and periprosthetic fracture (n = 2, one femoral, one tibial).
The femoral stem (3 cases) and the tibial stem (2 cases) as well as the tibial plateau and body (2 cases) could be replaced by MUTARS parts and conjoined with the remaining KMFTR devices. Three cases were converted to MUTARS total femur.
Postoperative complications were one aseptic loosening and one cone-dislocation. Pre-incidence function was restored in all cases. The average Musculoskeletal-Tumour-Society-Score was 82.9% of normal function.
The results show that the new adapter facilitates to restore pre-incidental extremity function by performing a relatively modest revision.

4.P.02

LONG TERM RESULTS OF UPPER LIMB SALVAGE WITH VASCULARIZED FIBULA GRAFT FOLLOWING RESECTION OF MALIGNANT BONE TUMOURS

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Following resection of primary malignant bone tumours of the humerus, limb salvage can be performed by vascularized fibula graft for reconstruction of large segmental defects.
In 12 patients with malignant bone tumour of the proximal humerus, tumour was resected and the bone defect reconstructed by vascularized fibula graft. Median age of the patients was 23 years. Median follow up was 114 months.
In 10 patients humeral head had to be resected and was replaced by fibular transplant including head and shaft of the ipsilateral fibula. Humeral head could be left in place in 2 patients. Median length of transplant was 17.2 cm. Radiographic union could be seen after 8 months in median. In 7 patients partial necrosis of the fibular head occurred, in 4 patients fracture of the transplant happened following trauma. In these 4 cases revision surgery was required. Partial necrosis of the head of fibula had no significant influence on shoulder function. One patient died of disease, the others are disease free. Enneking Index was 61% in median at time of last follow up. At donor side 3 cases of transient peroneal palsy could be seen.
We conclude that vascularized fibula graft is a successful surgical procedure for upper limb salvage especially for preservation of joint function also in long term follow up.

4.P.03

PRIMARY AND SECONDARY RECONSTRUCTIONS OF THE LOWER LIMB WITH GMRS® MODULAR PROSTHESES: IMPLANT SURVIVAL AND COMPLICATIONS IN A COMPARATIVE STATISTICAL ANALYSIS

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From October 2003 to September 2007 at Rizzoli 161 GMRS® prostheses were implanted after resections of the lower limb. This is a modular system with a knee rotating hinge mechanism, cemented and uncemented stems, in titanium and chromium-cobalt-molybdenum, curved and straight-fluted, with or without hydroxyapatite coating. Adaptors are available to revise HMRS® prostheses with hybrid implants. This study includes 88 males and 73 females ranging in age from 9 to 80 years. Sites of reconstruction were 109 distal femurs, 19 proximal femurs, 1 total femur and 32 proximal tibias. There were 149 oncologic and 12 non oncologic diagnoses, including 96 primary reconstructions and 65 revisions for failures of previous reconstructions. Analysis of imaging and complications was performed and function assessed according to MSTS system. Kaplan-Meier curves were used to statistically evaluate implant survival.
At a mean follow up of 2.5 yrs. 106 patients are continuously NED, 31 NED after treatment of relapse, 7 AWD, 5 DWD. There were 10 major complications: 8 infections (4.7%) (5 in primary and 3 in secondary implants) and 2 aseptic loosenings (1.2%) (1 each). There were 9 minor complications requiring minor revisions. Comparative statistical analysis of implant survival showed no statistically significant difference between primary and secondary implants. Functional results were good or excellent in 95% of patients, without any poor.
Middle term results are promising with no breakages of implant components. Besides oncological cases, there are selected indications in non oncological settings, such as revisions of prosthetic or allografts failures. While a higher complication rate was expected in secondary implants, statistical analysis shows similar survival.

4.P.04

SHORT-TERM FOLLOW UP OF JOINT SPARING PROXIMAL TIBIAL REPLACEMENTS

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The proximal tibia is the second most common site for primary bone tumours. As a result of simultaneous advances in chemotherapy, surgical and biomechanical techniques limb salvage is now a practical option. We report the clinical and functional outcomes of eight patients who underwent limb salvage with a new form of endoprosthetic proximal tibial replacement that allows preservation of the knee joint.
A retrospective, case series of 8 patients who underwent joint sparing proximal tibial replacement between 2004 and 2008. There were 2 males and 6 females with a mean age of 28.9 years (8-43) with overall mean follow up of 35 months (4-48). Functional outcomes were assessed using the Musculoskeletal Tumour Society (MSTS) rating score and revised Oxford Knee Score (OKS)
Five patients had osteosarcoma, one patient had malignant fibrous histiocytoma, another adamantinoma and the final patient had Ewing's sarcoma. All patients had complete tumour excision, neoadjuvant chemotherapy and to date there have been no distant metastasis.
One patient however required a below knee amputation through the prosthesis due to local recurrence at the distal bone/prosthesis interface. Another patient fell at postop day 8 and fractured through the tibial metaphyseal bone requiring ORIF; this healed in extension and ultimately required revision to a proximal tibial replacement 20 months later. Mean MSTS and OKS for the remaining 6 patients were 77% (57-90) and 40 (36-46) respectively.
Limb salvage preserving the knee joint is an effective alternative to a proximal tibial replacement when the metaphyseal bone is tumour free. The joint sparing prosthesis has a favourable functional result when compared to the joint sacrificing prostheses. Retaining the native joint improves functional outcomes and reduces the peak loads through the prosthesis. There was no short-term evidence of loosening. Further follow up is required to ascertain the long-term outcomes of this new prosthesis.

4.P.05

DISTAL RADIAL ENDO-PROSTHETIC REPLACEMENT- A WASTE OF TIME?

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Malignant tumours of the radius compose only 3% of all upper limb tumours. Owing to their rarity they are often difficult to manage satisfactorily. Of the options for fixation available, endo-prosthetic replacements have been scarcely utilized despite their success in limb preservation with malignant tumours in other parts of the body. At our centre we have used these when biological solutions (eg fibula graft) were not indicated due to extensive disease or the need for radiotherapy. We performed four endoprosthetic replacements of the distal radius in three males and one female with ages ranging from 19-66 years (average= 42.25 years of age). Two were performed for varieties of osteosarcoma (parosteal and osteoblastic osteosarcomas), one for a large destructive giant cell tumour (GCT) and one for destructive renal metastases. Three were right sided (75%) and one left sided (25%).
Medical records were evaluated for information on local recurrence, metastases, complications and functional outcome using the Toronto Extremity Salvage Score (TESS). Follow up ranged from 22 to 205 months (average= 116.5 months). The average TESS score was 58.1% (range= 44.6-74.5%). Neither case of osteosarcoma recurred. The GCT recurred twice and the patient with renal metastases had nodules removed from his affected wrist on two further occasions. There were no cases of infection, but the two earlier cases had problems with metacarpal stems cutting out and joint subluxatinos. The two earlier cases have since died at 205 (parosteal osteosarcoma) and 189 months (GCT) respectively of other disease.
We conclude that although this is a very small series of endoprosthetic replacement of the distal radius, the technique is a useful addition to the surgical options, with acceptable post-operative functional results and complication rates when a biological solution or preservation of the wrist joint is not indicated.

4.P.06

ALLOGRAFT-PROSTHESIS COMPOSITE RECONSTRUCTION AFTER INTRA-ARTICULAR PROXIMAL TIBIA RESECTION FOR BONE TUMORS

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Proximal tibia reconstruction after oncologic resection is challenging due to bone stock and extensor mechanism restoration.
From 1997 to 2007 19 patients (mean age: 39±16 years old) underwent proximal tibia oncologic intra-articular resection with wide margins. Primary diagnosis included giant cell tumor, osteosarcoma, chondrosarcoma and a failed osteoarticular allograft in 10, 4, 3 and 2 patients respectively. Tibial resection length was 10.4±3.4 cm in 18 knees. In one patient with chondrosarcoma the entire tibia was resected. Three patients received preoperative and postoperative chemotherapy, one only postoperative.
Reconstruction was performed with an allograft-prosthesis composite implant and direct suture of the host patellar tendon to the allograft one. Fresh frozen allograft and modular Link prosthesis were used for reconstruction. Five to six weeks of knee immobilization in extension followed the operation. A transient peroneal nerve palsy was observed in three patients.
Two patients with a stiff knee underwent an open release after less than one year from index surgery. One patient had a local recurrence from osteosarcoma and underwent an above knee amputation. No patient developed distant metastasis at follow-up.
After 59±37 months none of the patients had implant revision for mechanical complications. One patient had 2-stage implant revision for deep infection. A minor allograft resorption with aseptic drain was observed in one patient who underwent surgical debridement. One other patient had a moderate allograft resorption. Knee flexion was 96±12 degrees. All the patients but two could reach complete knee extension and only two had a minor extensor lag (less than 15 degrees).
In conclusion intrarticular tibia resection and allograft-prosthesis composite replacement ensures satisfactory oncologic and functional results at a mid-term follow-up.

4.P.07

DISTAL FEMUR RECONSTRUCTION WITH MUTARS ENDOPROSTHESES IN 28 PATIENTS WITH MALIGNANCIES

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A retrospective study focusing on long-term follow up of 28 patients with a malignant bone tumour in the distal femur was conducted. Patients with a mean age of 50 (18-90) were clinically and radiologically followed-up for a mean period of 64 months (7-144). Osteosarcoma was the most common primary bone tumour, occurring in 15 patients. The 5-year survival for all patients was 80,9%. At final follow-up, 19 patients were still alive and had a mean follow up of 74,6 months (7-137).
Clinical evaluation was done with the MSTS questionnaire (mean score: 70,0 (26,7-93,3)) and the use of the TESS (mean score: 82,5 (45-99,2) and SF-36 (mean Physical Component Score (PCS): 46,6 (27,1-56,5), mean Mental Component Score (MCS): 53,7 (range 37,0-62,1) was introduced
There were 12 complications: 5 aseptic loosenings, two deep prosthetic infections, two luxations, one prosthetic fracture and two fissures. Six failures were re-operated. An overall prosthetic survival at 5-years of 77,0 % was found. A total of eight (29%) prostheses were considered to have failed after a mean follow up of 27,4 months (0-97). Risk factors in failure of the prosthetics were: non HA-coated stem and top stem-ratio >1.2. Not length of the endoprosthesis and base stem-ratio. The top-ratio had a mean value of 1,14 (1,00-1,52) and for the four patients with an aseptic loosening the mean top-ratio was 1,23 (1,12-1,51) which was significantly different ($p<0,05$ Mann-Whitney U test).
Our results suggest that of the MUTARS endoprosthesis has a good 5-year survival.
The use with a HA coating is preferable. The use of a stem-cortex ratio (>1.2) at the top of the prosthetic stem can be predictor for aseptic loosening. The addition of the TESS and SF-36 scores give more insight information in how patients undergo their disease: half do not feel disabled.

4.P.08

DISTAL FEMORAL GROWTH PLATE FUNCTION FOLLOWING USE OF JOINT-SPARING ENDOPROSTHESES FOR TREATMENT OF DISTAL FEMORAL BONE TUMOURS IN CHILDREN OF BONE GROWING AGE

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Following resection of tumours in the distal femur, reconstruction with joint-sparing prostheses have shown good short-term functional outcomes. There is however limited literature on the affect of knee-sparing prostheses on function of the distal femoral physis in children of bone growing age.
We discuss two patients, a male (11yrs) and female (10yrs) who had joint-sparing distal femoral prostheses inserted for treatment of Ewing's sarcoma. The knee joint, along with the distal growth plate, was preserved and fixed to the distal end of the prosthesis using unicortical screws positioned distal to the physis. In the female, these screws were removed 6 months post-op due to prominence of the screws under the skin. In both patients, we assessed radiographs from immediately post-surgery and the most recent follow-up (20 and 28 months respectively). In each set, for the operated limb, we measured the height and width of the distal femoral epiphysis, the total length of the femur and the length of the proximal femoral bone segment from the femoral head to the proximal bone-prosthesis interface. In addition, post-operative assessments of leg lengths, bilaterally, were documented.
In both patients, distal femoral epiphyseal height and width in the operated leg showed no significant change following endoprosthetic replacement. In the female, growth did not resume even after removal of the epiphyseal screws. In both patients, lengths of the femur and the proximal bone segment increased significantly following surgery. The patients demonstrated no clinical leg length discrepancy at the most recent follow-up.
This study suggests that the function of the distal femoral growth plate ceases following insertion of joint-sparing distal femoral endoprostheses, probably due to trans-physeal fixation. This does not appear to resume following early removal of distal screws. The proximal growth plate, however, continues to function adequately enough to maintain symmetry in overall leg length.

4.P.09

MODULAR DISTAL FEMORAL REPLACEMENT FOLLOWING BONE OR SOFT TISSUE TUMOUR RESECTION – CLINICAL AND RADIOLOGICAL LONG-TERM-FOLLOW-UP

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Objective: Modular tumour prostheses are often chosen for the reconstruction of osseous or joint defects following wide tumour resection in limb salvage procedures. In this retrospective trial we were looking for the clinical use in accordance to long-term-follow up especially on aseptic loosening of stem, wear of polyethylene, implant related complications and clinical and functional results.
Methods: From 1996 to 2008 we performed in our clinic in 69 cases a modular distal femur replacement (MUTARS) after wide bone or soft tissue tumour resection.
In our outpatient clinic we have assessed the clinical follow-up as clinical examination (Enneking-score) and standardized radiological follow-up for 5 years, then once per year. In the focus of interest were aseptic loosening of the stems, wear of polyethylene, and mechanical problems as implant failure
Results: In long-term-follow-up 6 polyethylene locks had to be changed into PEEK locks (8,6%9). PEEK-lock complications were not seen in this series. In 5 cases late infection of the prosthesis occured. In another 5 cases aseptic loosening of the prosthesis was diagnosed, fractures of the stems were not seen.
We conclude that in tumour patients with major osseous reconstruction after wide resection a certain loss ob function cannot be avoided, but the rate of complications in the long-term-follow-up after implantation of modular tumour prosthesis is acceptable.

4.P.10

CUSTOM MADE INDIVIDUAL ENDOPROSTHESIS REPLACEMENT OF DISTAL RADIUS AFTER TUMOR

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There are results of our first experience treatment 8 patients who underwent endoprosthetic reconstruction of distal radius after excision of malignant tumors. All patients were treated in Sytenko Institute from 2004 to 2008 and had about 5 years follow-up. There are 3 males and 5 females and the median age at diagnosis was 36 (17-55) years. The resection length measured a mean of 8cm and was measure by radiographs, CT and MRI. Each case was malignant Giant cell tumor. There were 5 cases of primary tumor and 3 cases of local tumor relapse. The patients have had chemotherapy, tumor excision and individual custom-made endoprosthetic reconstruction. Unfortunately all patients had one-two surgeries before treatment in our Clinic. We used author's individual custom-made endoprosthetsis which was performed from titanium and ceramic spraying. CT-measurement scale was used for preoperative planning and manufacture this distal radius prosthesis.
One patient has had deep soft tissue infection and we were needed to remove prosthesis. One more patient had proximal radius fracture 4 month after surgery and we performed bone plate osteosynthesis. All patients (except one infection case) have satisfactory wrist range of motion and functional result of upper limb from 10 month to 5 years follow-up.
It is proved that surgical procedure of the tumors of distal radius is a useful and main method of the treatment above-stated localization. The individual custom made prosthesis have a good perspectives for upper limb salvage surgery and reconstruction this area, allowing to receive good oncological and functional results.

4.P.11

CUSTOM-MADE DIAPHYSEAL REPLACEMENT OF FEMUR AND HUMERUS

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Objective: To evaluate outcome parameters after custom-made diaphyseal replacement of femur and humerus in long term allograft failures.
Methods: A subset of osteo allograft reconstructions after tumour resection ultimately will fail in patients achieving long-term survival. The reasons for original allograft failure were fractures, osteonecrosis or delayed bony ingrowths and implant loosening (plates, nails).In this study patients had a failed massive allograft after tumor resection of humerus or femur. Alternative surgical approach to revising these reconstructions are endoprosthetic revisions to preserve limb function with minimal complications due to custom made modular diaphyseal replacement systems of femur or humerus, especially with short proximal or distal intramedullary anchoring.
Results: A series of custom made diaphyseal replacement systems of femur or humerus was done in our department demonstrating the feasibility of this technique. Most patients initially were treated because of malignant bone tumors like Ewing sarcoma or soft tissue tumours. Allograft fractures occured up to 49 month after initial tumour resection. The follow up included radiographic and clinical parameters. In all cases limb salvage, good function and pain relief was achieved.
Conclusion: Reconstruction of the diaphyseal aspect of the femur or humerus after failure of osteoarticular allograft with custom made diaphyseal replacement of femur and humerus is a good option to achieve limb salvage, good function and pain relief.

4.P.12

ENDOPROSTHETIC REPLACEMENT IN CHILDREN AND ADOLESCENTS WITH LONG BONE SARCOMAS: EXPERIENCE FROM ONE INSTITUTION

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Purpose: Function of the extremity assessment in children and adolescents treated with endoprostheses for bone sarcomas.
Method: We studied the results of the endoprosthetic replacements in 26 patients 5-17 years old (med-12,8) with malignant primary tumors: osteosarcoma (20), Ewing sarcoma (2), chondrosarcoma (3), rhabdomyosarcoma with bone affection (1). The surgeries were provided in 2004-2008 years for the joints: knee (19 - femur (10), tibia (9)), coxofemoral (2), humeral (4), elbow (1). We used non-expandable endoprostheses in 10 patients 13-17 years (med -15,3) and expandable ones in 16 patients 5-15 years (med-1,1): PROSPON (10), MUTARS (14) and REPIPHYSIS (2). Invasive lengthening was held for PROSPON (8 procedures in 5 patients) and noninvasisve for MUTARS and REPIPHYSIS (8 patients). All the patients underwent protocol therapy. The term of observation was 0,5-4,5 years (med-2,1). For low extremity good function was assessed as the ability of walking with ease, equal length of two legs and sufficient artificial joint's mobility. For upper extremity good function was assessed as the ability of using an arm freely in daily life (including writing and typing), equal length of two arms and sufficient artificial joint's mobility.
Results: 18 patients (69,2%) are alive. Local relapse had place in 1 (3,9%) case. Good function of an extremity was registered in 14 (73,7%) patients who survived. The best results we saw in noninvasive maintaining equal limb length.
Conclusion: Endoprosthetic replacement in a complex with protocol therapy secures good function of an extremity in children and adolescents with malignant primary bone sarcomas.

4.P.13

COMPARATIVE ANALYSES BETWEEN INDIVIDUAL AND MODULE ENDOPROSTHESIS

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The aim of this study was to analyze complications and functional outcomes after individual and module endoprosthesis.
From 1993 to 2008 in our clinic 42 patients with bone sarcomas were treated with resection and endoprosthetic reconstruction of large joints. In 29 patients we have applied individual, in 13 patients module prosthesis. We have assessed complications and functional results. For individual prosthesis: pyoseptic complications-4 (9,52%) pts, orthopedic events-9 (21,43%) pts, local recurrences-5 (11,90%); functional results: „excellent"-10,34% (3/29), „good"-48,28% (14/29), „satisfactory"-24,14% (7/29), „non-satisfactory"-17,24% (5/29). For module prosthesis: Only in one patient local recurrence has been observed. Functional results are so: „excellent"-23,1% (3/13), „good"-69,2% (9/13), „satisfactory"-7,7% (1/13), „non-satisfactory"-0.
We conclude that using of module endoprosthesis allows achieving good functional results with low rate postoperative complication.

4.P.14

THE COMBINED USE OF RECYCLED BONE AND VASCULARISED FIBULA IN LIMB-SALVAGE SURGERY FOR MUSCULOSKELETAL MALIGNANCIES – THE BONE IN THE BUN TECHNIQUE (HOT DOG TECHNIQUE)

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Autografts produced by recycling of tumor-bearing bone have been used for bridging intercalary bone defects but they are known to act as massive allografts after recycling procedures due to devitalisation. Recycled bone is superior to massive allografts since it allows anatomical reconstruction.Vascularised fibular grafts are inserted into recycled bone segments to provide biological support and to promote healing.
Twelve patients with a mean age of 13.3 years (6-31), who had undergone curative resection of malignant bone tumor followed by biological reconstruction comprised of recycled bone combined with vascularised fibula, were followed up for a mean period of 16.8 (6-46). The tumor was located in distal femur in 7 patients, proximal femur in 2, proximal tibia in 2 and mid-diaphyseal tibia in 1. Cryopreservation with liquid nitrogen was employed for all patients. Contralateral single strut vascularised fibular grafts were used in all except one patient for whom bilateral fibula grafts were harvested to span a longer defect. Plates were used for fixation in 11 patients, and intramedullary nailing in one case. Mean length of bony defect was 16.1 cm (9.0-25.0). Mean fibular graft length was 17.5 cm (10.0-23.0 cm).
Complete union and full weight bearing was achieved in 6 patients, and mean time to detect the commencement of union was 6 months (4-8). Incomplete union was detected in 4 patients and no union in 2. Five patients were complicated by implant failure, 1 with deep infection and 1 with drop foot.
In order to fill large defects after resection of bone tumors, recyled bone combined with vascularised fibular graft is an effective reconstructive tool. Union rate of this technique is quite satisfactory with good functional results.

4.P.15

COMPLICATIONS OF BIOLOGIC RECONSTRUCTION SURGERY FOR TREATMENT OF CHILDHOOD MALIGNANT MUSCULOSKELETAL TUMORS

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In an era where the survival rates of oncologic patients are improving, biologic reconstruction is the treatment of choice, however, it has its complications and fortunately we have the solutions. Biological reconstruction was performed on 52 patients with a mean age of 11.3 (1.5-16) after malignant bone tumor resection in our institution between 1991 and 2008. Patients were followed up for a mean period of 49 months (3-216). Twenty-nine patients were diagnosed with osteosarcoma, 22 with Ewing sarcoma and 1 with adamantinoma. A wide range of vascular and nonvascular autografts, allografts, fibular transposition, bone regeneration and bone recycling techniques were utilised alone or in combination for reconstruction. Crucial anatomical parts (epiphyses, apophyses, triradiate cartilage, glenoid) were preserved in 41 patients while maintaining safe surgical margins.
Wound problem was the most common early complication. The most common late complications were nonunion, limb length discrepancy, limitation of range of motion (ROM), deformity, implant or external fixator failure and fibular graft fracture. Local recurrence was seen in only 2 patients. Patients underwent a mean of 0.8 (1-10) additional surgical interventions for treatment of complications. Thirty-one out of 43 lower extremity patients became ambulatory with full weight bearing and near full ROM while 4 died of disease and 2 were disarticulated prior to healing or treating of complications. Six patients with reconstructions around the glenohumeral joint had functional outcomes varying from excellent to poor with defect pseudoarthrosis. Two patients with successful pelvic reconstructions suffered from co-morbidities and disease itself. Implants and fixators, orthoses, physiotherapy and antibiotherapy were used as necessary for treatment of complications.
Biologic reconstruction yields good functional outcomes and allows more flexibility while treating complications since it preserves bone stock and epiphyses.

4.P.16

THE USE OF IRRADIATED AUTOLOGOUS BONE IN JOINT SPARING ENDOPROSTHETIC REPLACEMENT TUMOUR SURGERY

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The use of massive endoprostheses following bone tumour resection is well recognised. Where possible, joint salvage rather than joint replacement is usually attempted. However cases arise where there is insufficient bone following tumour resection to allow adequate fixation of a joint sparing prosthesis. We report a series of 4 patients (aged 4-12), treated between 1994 and 2008, in which irradiated autologous bone has been combined with a diaphyseal or distal femoral replacement in order to preserve the native hip joint.
There were 3 cases of osteosarcoma and 1 case of Ewing‘s sarcoma. After a mean follow-up of 53.5 months (range 9-168), all four patients are alive without evidence of local recurrence or metastases. One implant was revised after 14 years following fracture of the extending component of the growing endoprosthesis. There have been no cases of loosening or peri-prosthetic fracture.
This is the first report of irradiated autologous bone with joint sparing endoprostheses in skeletally immature patients.

4.P.17

HIP ARTHRODESIS USING A VASCULARIZED FIBULAR GRAFT AFTER PROXIMAL FEMORAL RESECTION FOR PRIMARY MALIGNANT BONE TUMOURS

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Fifteen patients (11 males, 4 females) with a median age of 16 years (range, 7-25) were treated in our centre by intra-articular resection of the proximal femur, and hip arthrodesis using a vascularized fibular graft. Eight patients had Ewing's sarcoma, 5 osteogenic sarcoma, and 2 chondrosarcoma.
After a mean follow up of 58.2 months, 13 patients were alive with no evidence of disease. All fibular grafts united at a mean time of 7.6 months (range, 7-9 months). Four patients had stress fractures of the vascularized fibular graft, all healed after a mean period of 6.5 weeks. Failure of the fixation system occurred in two patients. Deep infection developed in one case which necessitated plate removal. Three of these patients with complications underwent a second procedure, giving a re-operation rate of 20%. The mean MSTS functional score was 85.9% at the time of the latest follow-up.
We conclude that hip arthrodesis using a vascularized fibular graft is a viable alternative to endoprosthetic replacement after proximal femoral resections. It should be considered as an effective and durable reconstructive technique in young patients with high physical demands.

4.P.18

LONG TERM FOLLOW-UP RESULTS AFTER RECONSTRUCTION BY DISTRACTION OSTEOGENESIS FOLLOWING BONE TUMOR RESECTIONS

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The authors aim to report the long-term follow-up experience in the reconstruction of bony defects by Ilizarov's distraction osteogenesis using bone transport method following en bloc resection of bone tumors.
En bloc resection was performed nine patients with bone tumors between October 1991-January 2000. The mean age of the patients was 19.3 years. Histological diagnosis was osteosarcoma in four cases, Ewing sarcoma in two cases, giant cell tumor (aggressive) in one, osteofibrous dysplasia (latent) in one and osteoblastoma (aggressive) in one case.
The average follow-up period was 122 months and bone defect after resection was 14 cm. The function of the affected leg was excellent in four patients, good in two and poor in one patient according to the modified system of the MSTS. In the case where reconstruction of the ulna was done, MSTS score was excellent and DASH skoru was 2.5.
We imply that in patients with long life expectancies, reconstruction with distraction osteogenesis seems to be an efficient method in the long-term follow up, on condition that its complications are promptly managed.

4.P.19

TREATMENT OF LEGS DISCREPANCY WITH EXTERNAL FIXATORS IN YOUNG PATIENTS: LONG TERM OUTCOME AFTER BONE TUMOUR SURGERY_

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Conservative treatment of neoplastic bone lesions in paediatric patients may require the sacrifice of growth cartilage with subsequent hypometria or axial deviation of the lower limb.
Segmental reconstructions can be made using acrylic cement and intramedullary nailing or allograft. In case of involvement of the joint, reconstruction can be performed with prosthesis or arthrodesis.
These reconstruction techniques can lead to a progressive deformity associated with shortening of the limb.
The resolution of legs discrepancy and axial defects in survived patients often requires more than one surgical procedure.
In our Institute, the patients affected by aforementioned defects, are treated with axial or circular external fixator at completed skeletal growth.
This paper refers complications and outcomes in five patients treated:
1st case. Male, 10 years: osteosarcoma of the distal femur healed with residual shortening of 8 centimeters.
We proceeded with a double level lengthening (proximal femur and proximal tibia) using Ilizarov technique.
2nd case. Female, 8 years:distal femur osteosarcoma healed with a shortening of 6,5 centimeters. We used the Ilizarov apparatus to achieve an elongation of cm. 7 on soft tissues allowing the subsequent bone replacement with allograft of appropriate length.
3rd case. Female, 9 years: Ewing sarcoma of the femoral shaft. The correction of the legs discrepancy (8 centimeters) was performed using the Ilizarov apparatus with a proximal tibial corticotomy.
4th case. Female, 11 years: distal femur osteosarcoma healed with residual shortening of 8 centimeters.
A gradual lengthening of soft tissues with recovery of the length leg allowed the insertion of a new allograft associated with vascularised fibula.
5th case. Male, 13 years: femoral fracture in fibrous dysplasia. Residual leg discrepancy of 5 centimeters treated with tibial lengthening by a proximal corticotomy and use of the Ilizarov apparatus.
The results obtained in our patients show that the use of the external fixator increases the quality of life in long-term survivors.

4.P.20

MULTISEGMENTAL PRIMARY TUMORS AND SOLITARY METASTASIS OF THE THORACOLUMBAR SPINE: RESULTS BY MANAGEMENT WITH MULTILEVEL EN BLOC SPONDYLECTOMY AND RECONSTRUCTION USING A CARBON COMPOSITE VERTEBRAL BODY REPLACEMENT SYSTEM

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Introduction: Total en bloc spondylectomy (TES) as the only radical treatment option for sarcoma and solitary metastases of the spine was shown to markedly minimize local recurrences, improve patient quality of life and substantially increase overall survival rates. Due to surgical difficulty of TES and complex biomechanical demands in defect reconstruction multisegmental tumor involvement of the spine has long been considered as a palliative situation, exceeding the limits of surgical feasibility. Thus, multilevel resections reports are very rare. For the first time, this study analyzes the onco-surgical results after multilevel thoracolumbar TES and reconstruction with a carbon composite vertebral body replacement system (CC-VBR) in a collective of patients.
Methods: 18 patients (9f/9m; age 52±14y) treated with thoracolumbar multilevel TES (6x2, 9x3, 3x4 segments) for spinal sarcomas (n=9), solitary metastases (n=5) and aggressive primary tumors (n=3) were retrospectively investigated. According to the classification system of Tomita et al. all patients were surgically staged as type 6 (multisegmental/ extracompartimental). Defect reconstruction (11 thoracic, 3 thoraco-lumbar and 4 lumbar) were performed with posterior stabilization and a CC-VBR. Patient charts and the current clinical follow-up results were analyzed for histopathological tumor type, pre- and postoperative data (symptoms, duration of surgery, blood loss, complications, intensive care, adjuvant therapies etc.) and course of disease. Latest radiographs and CT-scans were analyzed at follow up. Oncological status was evaluated using cumulative disease specific and metastases-free survival analysis.
Results: With a mean follow up (100%) of 18 (4-44) months 17 patients (94%) were postoperatively ambulatory without any support. Postoperative neurological deficits were seen in one patient (6%). Wide resection margins were attained in 7, marginal in 11 patients. Depending on tumor biology/grading and/or resections margins an adjuvant therapy (radiation/chemotherapy) was performed in 12 (67%) patients. Local recurrence was found in one patient (6%). 13 (72%) patients showed no evidence of disease, 3 were alive with disease while 2 died of disease at 10 and 27 months postoperatively.
Conclusion: In selected patients with multisegmental spinal tumor involvement oncological sufficient resections can be reached by multilevel TES. Although the surgical procedure is challenging and the patient`s stress is considerable our encouraging midterm results together with the low complication rate clearly favour and legitimate this technique. However, treatment success strongly depends on adjuvant therapies. Reconstruction with a CC-VBR showed low complication rates, promising biomechanical characteristics, increased volume for bone grafting and lower artefact rates in follow-up MR- and CT-imaging.

4.P.21

OSTEOPLASTY, VERTEBROPLASTY AND RADIOFREQUENCY THERMAL ABLATION IN TREATMENT OF PATIENTS WITH TUMORAL DEFEAT OF BONES

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Purpose: estimate efficiency minimally invasive methods of treatment at patients with tumor lesion of bones.
Materials and methods: 145 patients, middle age e 42 years. it has been executed 249 percutaneous vertebroplasty, 15 osteoplasty and 46 radiofrequency thermal ablation Most often minimally invasive methods were carried out to patients with bone metastasis lesion of a breast cancer - 65 (44,8%) and kidneys - 14 (10%) patients.
Results: reduction in a painful syndrome on a visual analog scale after operation is noted at 126 (87%) by patients. Positive dynamics Watkins scale at 119 (82%). Improvement of quality of a life on scale Karnofski at 94 (65%) the patient. Complications after vertebroplasty and osteoplasty in the form of methylmethacrylate leak into the surrounding tissues at 19 (18,5%) patients. At one patient after radiofrequency thermal ablation has developed burn skin. There were three pathological bone fractures after radiofrequency thermal ablation.
Conclusions: vertebroplasty, osteoplasty and radiofrequency thermal ablation - minimally invasive methods of treatment the patients with tumoral lesion of the bones, allowing in short tim stop a painful syndrome, create adequate stability in a bone segment and improve quality of a life of oncological patients.

4.P.22

FOLLOW-UP OF SARCOMA BY ULTRASOUND

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Detection of local recurrence after sarcoma resection can be impaired by metal implants locally, or by the patient ‘s general condition. Metal implants cause severe distortion and scattering of either MRI or CT data acquisition. Therefore the detection of local recurrences in proximity of heavy metal implants such as prostheses or osteosynthesis material can be difficult. Patient related conditions, e.g. renal insufficiency, allergy, claustrophobia, may completely prohibit the use of contrast media or even a scan itself.
Ultrasound provides several advantages, and can be used for different indications in sarcoma patients. Patient related conditions prove no obstacle for this technique. Currently our indications are local follow-up after soft-tissue sarcoma resection and evaluation of regional lymph nodes, detection of local recurrence of bone sarcoma in proximity of metal implants, and amputation stump evaluation.
We describe a patient study population of 103 patients. Seventeen had only diagnostic and staging ultrasound, four had an evaluation of their amputation stump, 24 were followed after resection of a soft-tissue sarcoma, and 58 were followed by this method after sarcoma resection and implantation of metallic implants. Evaluation modalities are described according to the indications.
Results: We have detected nine local recurrences, and four patients with suspect lymph nodes had a biopsy of which half showed malignant tumour cells. Infection and inflammation around metallic implants can be evaluated, the technique also allowing placement of drains in infected seromas in irradiated regions. It should be emphasised that reliable results can only be achieved if a baseline ultrasound is performed, followed by subsequent studies at regular intervals.

4.P.23

FOCAL NODULAR HYPERPLASIA OF THE LIVER FOLLOWING SOLID TUMORS IN CHILDHOOD

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The detection of hepatic nodules during follow-up of survivors of solid tumors in childhood raises a diagnostic dilemma. Focal nodular hyperplasia (FNH) is an uncommon, benign tumor and must be differentiated from late hepatic metastasis.
We retrospectively analyzed patients, treated for pediatric solid tumors between January 1990 and December 2007, and performed abdominal imaging as part of the follow-up.
Four survivors with FNH were detected, out of 450 who received chemotherapy with/out irradiation including patients who underwent autologous bone marrow transplantation (ABMT).
Case 1: A 23 years(y) adolescent, presented at age 10y with acute abdomen due to embryonal sarcoma of liver, she received VACAIEx4, relapsed locally, and underwent ABMT with high-dose carboplatin/melphalan and radiotherapy. Asymptomatic multiple liver lesions were disclosed by US and MRI 5y later, biopsy proved FNH. Case 2: A 21y adolescent who at age 3y had alveolar rhabdomyosarcoma of the calf with positive inguinal nodes. She received VACAIE x6, and VP16/carboplatin x3 with local radiation. She developed ovary disorder and received oral contraceptive (OC) at age 14.5y, routine US 1.5y later disclosed nodular lesions in liver, diagnosed as FNH by CT, pills were stopped. At follow-up some lesions reduced in size and few disappeared. Case 3: A 9y old girl, operated for choroid plexus carcinoma at age 1.5y, received VP16/carboplatin x16 and underwent ABMT preceded by thiotepa/melphalan. Abdominal US at age 5.5y disclosed multiple liver lesions, biopsy proved FNH, that disappeared 2y later. Case 4: An 11y old girl operated at age 8 months for retroperitoneal germ cell tumor, received VIP/BVPx4, routine US at 10y disclosed 2 liver lesions diagnosed byWe conclude that FNH can be differentiated from late metastasis by imaging; in questionable cases by biopsy, close follow-up is recommended, alkylating agents especially during ABMT, and OC may be risk factors.

4.P.24

LONG TERM FOLLOW-UP IN ADULT PATIENTS TREATED FOR BONE SARCOMA IN PEDIATRIC AGE

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From January 2003 a long term follow-up project started for adult patients treated in our Centre for cancer in pediatric age, to evaluate late effects of therapy. For all patients a personalized follow-up was scheduled (time, function-tests, etc).
We analyzed 24 cases of bone tumors: 14 osteosarcoma (OS) and 10 Ewing's sarcoma (ES). Median age at diagnosis was 13 years (range 11-18) for OS patients, 11.6 years (range 6-18) for ES; 50% males in both groups. All patients were treated according current CNR/ISG-protocols: all OS cases underwent surgery; in 5/10 ES patients local treatment was surgery, in 5/10 radiotherapy; 7/24 received hematopoietic stem cells transplantation (HSCT).
Median age at evaluation is respectively 26.5 years (range 18.7-34) and 23.5 (range 21.6-32); median follow-up is 13 years (range 6-22) and 13.7 (range 6.7-22.3).
Cardiovascular function is normal in all OS cases; 3/10 ES patients developed asymptomatic ejection fraction reduction, currently not treated.
One OS patient underwent bilateral thoracotomy and HSCT for multiple metastases at diagnosis and had a mild lung function alteration. One OS patient developed mild chronic kidney disease, one ES nephrolithiasis. Liver function is normal in all cases.
Height velocity and final height are normal in 10/14 OS and 9/10 ES patients; in remaining 5/24 no growth hormone secretion deficit was found.
One OS patient developed primitive hypothyroidism and one OS benign thyroid nodule with partial thyroidectomy; one patient multifocal papillary thyroid carcinoma with total thyroidectomy at 11 years from diagnosis of ES.
Spermatogenesis deficit is a common find (5/7 OS and 5/5 ES male patients); one female treated with HSCT and radiotherapy for ES pelvic relapse has primitive hypogonadism. No other hypothalamo-hypophyseal-adrenocortical system hormones deficit was found.
We reported no significant neuropsychological alterations nor employment problems: 20/24 patients have a job, 4/24 are students. Three OS females have children.

4.P.25

OSTEOPOROSIS – A LATE EFFECT AFTER CHEMOTHERAPY FOR BONE SARCOMAS

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High-dose methothrexate, a standard agent in the therapy protocols for osteosarcoma, has long been suspected to have a negative long-term effect on bone metabolism and bone mineral density, especially in children and young adults. Recent literature questioned this association as also the BMD of Ewing's sarcoma patients treated without methothrexate is known to be decreased. We therefore wanted to screen our patients treated for Ewing's sarcoma and osteosarcoma for osteopenia/osteoporosis-associated fractures.
Between 1994 and 2008 107 patients below 50y of age were treated for bone malignancies including 51 Ewing´s sarcomas – 31 male and 20 female - with a mean age at diagnosis of 17y(±11SD) and 56 osteosarcomas – 36 male and 20 female - with a mean age of 23y(±12SD). We screened the patients' files for fractures after chemotherapy.
We found five patients with not trauma-associated fractures - one Ewing's sarcoma(1/51;2%) and four osteosarcoma patients(4/56;7%). They presented one fracture of the proximal femur 107 months after tumour diagnosis, three fractures of the distal femur after 29, 51, and 72 months and two fractures of the proximal tibia after 29 and 32 months (one patient suffered from fractures affecting both – the distal femur and the proximal tibia).
As presented in our case series fractures due to an osteoporotic process after chemotherapy for bone sarcomas are well known late effects. Although described in several studies therapeutic recommendations for prophylaxis are sparse. Furthermore the fact that fractures occurred in both types of sarcoma casts MTX as the main cause of chemotherapy-induced osteoporosis into doubt. Additionally we estimate a high number of unreported cases of premature osteoporosis because sarcoma patients are usually not tested for their BMD-levels. Therefore further studies using DEXA (dual-energy-x-ray-absorptiometry) to measure the patients BMDs after chemotherapy are needed.

4.P.26

QUALITY OF LIFE IN PATIENTS WITH OSTEOSARCOMA OF THE DISTAL FEMUR TREATED WITH CHEMOTHERAPY, RESECTION AND PROSTHETIC RECONSTRUCTION

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Osteosarcoma is a common primary bone sarcoma and distal femur its most frequent site. Between 2003 and 2008 at Rizzoli, 66 patients with osteosarcoma of the distal femur had neoadjuvant chemotherapy, resection and reconstruction with modular uncemented megaprostheses. Series included 37 males and 29 females. Mean follow up was 2 years. To measure "subjective" outcome Karnofsky scale (KPS) was assessed for each patient pre and post-treatment. Also a functional evaluation according to the MSTS system was performed. To find out the current quality of life, a questionnaire on life at work, study and sport before and after treatment was sent to 64 alive patients.
Before treatment 7 patients had a Karnofsky index (KI) of 60%, 31 of 50%, 25 of 40% and 3 of 30%. After treatment 19 patients had a Karnofsky index performance of 90%, 28 of 80%, 11 of 70%, 5 of 50% and 1 of 40%. Two patients died of disease. The most represented index of KPS after teatment was "Able to carry on normal activity; minor symptoms". Poor results were related with amputation (2), knee stiffness (3), infection (2), aseptic loosening (1). After treatment 91% of patients had a KI over 70%, while 89% a KI lower than 50% pre-treatment. MSTS system showed excellent or good results in 85% and fair or poor in 15% of the patients. Average score at MSTS evaluation was 22 (73%). Questionnaires (some still pending) confirm previous analysis.
KPS is simple and effective in evaluating quality of life in patients treated for distal femur osteosarcoma. In this study it confirmed the satisfactory MSTS assessed results. It is an easy method, useful and accessible for patients. The reported analysis shows that patients treated for osteosarcoma of the distal femur can have a good quality of life.

4.P.27

QUALITY OF LIFE, ACTIVITIES AND FATIGUE BEFORE AND AFTER THE TREATMENT OF BENIGN AND LOW GRADE MALIGNANT BONE TUMORS

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Nowadays more attention is paid to the quality of life during and after cancer treatment, and fatigue is an important factor influencing this. Still little is known about the development of fatigue before, during and after cancer treatment and its contributing factors. We analyzed the level of fatigue, pain, anxiety and activity before and after the treatment of benign or low-grade malignant bone and soft tissue tumours in 43 patients. All patients were treated with surgery only. The mean age of the patients was 40 years (range 20 to 67 years). Fatigue severity was measured with the CIS-fatigue questionnaire, where a score of 35 or higher reflects severe fatigue. The VAS score was used to measure pain (0=no pain, 10=severe pain), and the Dutch version of the Spielberger State-Trait Anxiety Inventory to measure state anxiety. Physical activity was measured with an actometer, worn at the ankle for two weeks. All measurements were done before the tumor surgery and twelve months later.
Severe fatigue was seen in 35% of the patients before they had tumor surgery. After 12 months 32% of the patients still was severely fatigued. The mean VAS pain score was 2,3 before treatment and 2,2 after 12 months. The anxiety score lowered from 38,1 before treatment to 33,2 one year later. Actometer scores increased from 57,7 before treatment to 69,9 after 12 months. Fatigue severity correlated with pain and anxiety both before and 12 months after treatment, but not with actometer scores.
In this study we see that severe fatigue is present in 35% of tumor patients before they are treated, and this percentage remains high (32%) until one year after surgery. Since severe fatigue correlated with more anxiety and pain, these symptoms can help us understand and treat severe fatigue in tumor patients better.

4.P.28

CHILDHOOD CANCER SURVIVOR STUDY- SINGAPORE, THERAPY REALTED TOXCITY IN LONG-TERM SURVIVORS OF OSTEOSARCOMA: EXPERIENCE IN SINGAPORE

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Childhood cancer survival has increased dramatically over the last 30 years. Childhood Cancer Survivor Study- SG was established to evaluate the outcome and toxicities experienced by long term childhood cancer survivors in Singapore. There were 429 cases of hematological malignancies (HM) and 342 cases of solid tumors (ST) diagnosed and treated at National University Hospital (NUH) Singapore from May 1981 to December 2007.
There were seven long term survivors for Osteosarcoma (OS) out of 26 patients seen during the study period. Median age at diagnosis was 13.8 (range, 6.4-15.8 years) and median follow-up was 7.9 (range, 2.6 – 13.2 years). Cumulative doses of chemotherapy received included: cisplatin (240 – 800 mg/m2); doxorubicin 150 – 450 mg/m2); methotrexate (16 – 144 Grams/m2); ifosfamide (27-80 mg/m2); and etoposide (1000 – 3300 mg/m2). According to the NCI Criteria for Toxicity (CTC version 2.0), three patients experiences grade 2 sensorineural hearing loss; three cases of grade 1 cardiomyopathy; three cases of grade 1 renal tubulopathy; and six cases of post surgical complications (infection-3, length discrepancy-3, poor fitting prosthesis-2).
Many of the patients did not have baseline pre-treatment evaluations such as audiograms, renal function, echocardiograms and similar proportion were not adequately followed-up post treatment. This is the first analysis and report in the country on treatment related outcome and toxicity in long-term survivors of childhood cancers such as osteosarcoma and other solid tumors. Authors recommend that future treatment protocols for childhood cancer in Singapore should incorporate pre- and post-treatment evaluations and close follow-up of young survivors with establishment of a multi-disciplinary late effects clinic.

4.P.29

THE EXPERIENCE OF HGSA IN THE TREATMENT OF OSTEOSARCOMAS

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Osteosarcoma is the most common tumor among the primitive malignant bone tumors. When different features of these lesions are considered, we can find several varieties of this tumor, with distinct anatomo-clinical presentation, treatment and prognosis.
Until the 70s, its prognosis was very poor, the standard surgical treatment was amputation and 80% of the patients died from metastatic disease. With the development of new surgical techniques, the advent of combined chemotherapy and more accurate imaging, the outcome of these patients has improved significantly. Consequently, approximately 90% of the surgical cases are treated with limb salvage procedures.
The authors reviewed 22 cases of Osteosarcoma treated in HGSA, 20 being submitted to the T20 Rosen protocol.
Trocar biopsy was performed in 19 of the patients and 3 of the patients were submitted to incisional biopsy in order to complete diagnosis.
Regarding the anatomo-clinical pattern, Classic Osteosarcoma was present in 19 patients, 2 of the cases were Parosteal and 1 was Central low-grade Osteosarcoma.
The majority of patients underwent limb salvage surgery; only 2 had amputation surgery and 1 patient was submitted to palliative chemotherapy. Considering limb salvage procedures, several techniques were performed: arthrodesis (n=1), grafts (n=4), prosthesis (n=13) and compound prosthesis (n=1). The resection margins were wide in 19 cases, marginal in 2 cases and in 1 case intra-luminal.
Among the treated patients: 12 patients are still alive and cured, 3 have metastatic disease, 6 are deceased and 1 didn't complete the follow-up.
The final functional score obtained was 84% for the superior limb (DASH) and 81% for the inferior limb (TESS).
Although the scarce number of cases described were not enough to make any kind of correlation, it was possible to establish the accuracy of the multidisciplinary approach involved both in the diagnosis and treatment, in agreement with the "state of art".

4.P.30

OFFSPRINGS OF PATIENTS AFTER TREATMENT FOR OSTEOSARCOMA. WHAT DO WE POSSIBLY HAVE TO EXPECT?

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Rationale: Osteosarcoma predominantly affects adolescents and young adults. Reduced fertility in men is well documented following treatment for osteosarcoma and related to chemotoxicity.
We have however not found data about the health of children of patients formerly treated for osteosarcoma.
Among our few patients we have had one offspring with an infantile fibrosarcoma successfully treated with high dose chemotherapy and surgery. One mother has secondary gastric malignancy after successful pregnancy.
With this contribution we want to draw the attention to include data of children in the long-term implications of osteosarcoma and its treatment.
Materials and Methods: Patients: Of 75 patients with osteosarcoma 11 patients (5 women, 6 men) have 16 children ‚produced' after completed oncologic treatment
All women became pregnant as planned. There are no female patients evidently infertile. One man among our patients shows azoospermia and is infertile. One man with oliogespermia has a healthy daughter after successful vitro fertilisation.
All patients have had treatment for osteosarcoma after puberty.
Offsprings: Pregnancy and delivery were uneventful for all children. The one girl mentioned above at birth showed a tumor of the Plexus brachialis which was a biopsy proven infantile fibrosarcoma. She received high dose chemotherapy. Resection of the tumor retaining the brachial at 9 months of age showed only scarce tumor residuals; she is disease free at 4 years of age. Her two siblings are healthy
Conclusion: We want to stress that in follow up studies events during pregnancy and health of offsprings should be included.

4.P.31

FERTILITY IN FEMALE SURVIVORS OF NON METASTATIC OSTEOSARCOMA

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Increased intensity of therapy for osteosarcoma in the last 30 years has improved prognosis. 70-80% of patients with non metastatic osteosarcoma can now be cured, but late side effects occur. Fertility of survivors is becoming of greater importance.
We retrospectively studied all consecutive female long term survivors of localized osteogenic sarcoma of childhood and adolescence treated at the Schneider Children's Medical Center of Israel. Patients were treated with 3 different protocols including the use of Methotrexate, Adriamycin, Cisplatin, Bleomycin, Cytoxan, Vincristine, Actinomycin D, Melphalan and Ifosfamide. Sixteen female survivors of non metastatic osteogenic sarcoma were treated from 1/1977 to 12/2001, with a minimum follow up of 6.3 years (max. 29 years) from the end of therapy. Median age at diagnosis was 11.7 (range 9.0-16.8) years. Twelve out of 16 (75%) are married and have between them 31 children, mean 2.7 (range 1-7) children. Of these 11 have children and one is currently pregnant with her first child. None of the females reported difficulties in conceiving their first child. The maximum interval from marriage to first delivery was 2.5 years. Two females had 3 spontaneous abortions between the 2^{nd}-4^{th} pregnancies. Four out of 9 female survivors who received >360mg/m^2 of adriamycin were treated with cardiomimetic drugs and/or ACE inhibitors during pregnancy. All four had 2-4 children/ female survivor. The children of survivors are healthy with no birth defects. Mean length of pregnancy was 38.6 weeks and mean birth weight was 2865 grams. No survivors had undergone invasive fertility preservation procedure and only one unmarried patient was using GnRH analogs.
Despite reports of transient disturbances in menstruation, all married females were fertile. Our results question the need for fertility preservation using GnRH analogs or invasive procedures such as ovary or egg preservation for non metastatic osteogenic sarcoma female patients.

4.P.32

CISPLATIN TOXICITY IN LONG-TERM SURVIVORS OF OSTEOSARCOMA: EXPEREINCE IN SINGAPORE

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Childhood long-term survivors now experience significant late effects from the primary cancer itself or from therapy. Cisplatin, an alkylating agent used in treatment for osteosarcoma, has been associated with irreversible high-frequency sensorineural hearing loss. There were 27 osteosarcoma patients treated at Department of Pediatrics, National University Hospital from 1997 to 2005. Twelve of these were long-term survivors, i.e. survived more than 2 years from initial diagnosis.
Pre-chemotherapy audiogram was performed in 50% (n=6) of patients and the audiogram results were not available in the remainder (n=6, 50%) as it was either not done or records were not available. Prior to year 2003, Cisplatin was administered at a dose of 100mg/m^2/course (EOI regimen) in 50% of cases, and after year 2003, 120mg/m^2/course (T12 regimen) in 45%. Median cumulative dose of cisplatin was 550mg/m^2 (cumulative dose range, 240 – 800 mg/m^2). Out of 12 patients, 7 patients (58%) experienced cisplatin induced ototoxicity. According to NCI Toxicity Criteria, Grade I ototoxicty was observed in two cases (30%), grade 2 toxicity in five cases (70%), and bilateral sensorineural hearing loss was noted in six of the survivors. One long term survivor required a hearing aid. Six of them had and renal tubulopathy (NCI Toxicity Grade 2) was noted simultaneously in 35% of cases (n=4).
The incidence of cisplatin induced ototoxicity is high in our small series of long-term survivors of osteosarcoma. Baseline pre-chemotherapy testing, close monitoring during treatment and further follow-up are essential for this subset of patients receiving high doses of cisplatin.

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4.P.33

SUBCLINIC LIVER DYSFUNCTION IN CHILDREN WITH SARCOMAS OF BONES AND SOFT TISSUE

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Subclinic liver dysfunctions (SLD) wildly spread among adult oncology patients and can negatively influence to results of some oncology patients treatment. But information concerning same problem in children is remain lack.
The purpose of this investigation was the determination of SLD spreading among children with sarcomas of bone and soft tissues and estimation its clinical sigMaterials and methods: 200 children with sarcomas of bones and soft tissues were involved in the observation (136 boys and 64 girls) in age groups: 2-10 years - 86 and older 10 years - 114. All children were examined with the help of clinic and laboratory methods including biochemical, serologic and immunologic testing of the blood.
Results and discussion: Results obtained if the investigation demonstrated that different degree of the SLD was widely spread among children with sarcomas - biochemical signs of SLD were detected at 26.0% children. Frequency and degree of severity of SLD increased parallel with increasing the clinical stages of sarcomas.
Serological markers of infections caused hepatitis B and C viruses in all children had biochemical signs of SLD were detected in several times frequently than in all children had no above mentioned signs of subclinic hepatopathy.
Presence of SLD signs in children with sarcomas was accompanied with more expressed depression of immunologic reactivity including natural antitumor resistance estimated on the base of natural killer cells' cytotoxicity.
Besides, presence of biochemical signs of SLD in children with sarcomas was accompanied with more frequent and expressed side-effects of chemotherapy and lower effect of treatment of those children.
Conclusions: 1. SLD spread among children with sarcoma as like as among adult oncology patients. 2. Presence of SLD children with sarcomas has important clinical significance.

4.P.34

RENAL TOXICITY IN PATIENTS WITH EWINGS SARCOMA/PNET TREATED WITH HIGH DOSES OF IFOSFAMIDE

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Introduction: Late effects of treatment in pediatric oncology patients are major issues of follow up care. Success in overall survival of patients with Ewing´s sarcoma/PNET (ES/PNET) correlates with cumulative doses of alkylating agents especially. Renal toxicity is subject of interest due to irreversible tubulopathy and need of many concomitant nephrotoxic drugs given during treatment.
ObjectiveE: Patients suffered from ES/PNET on Euro Ewing 99 protocol were eligible for evaluation of renal functions during therapy and follow up.
Methods: Design ofthis study was single institution observational. Total of 20 patients were included 9 females and 11 males. Renal toxicity was assessed as glomerular filtration rate according to Schwartz´s formula (GFR), serum creatinine (S-crea), fractionated phosphate reabsorption (T_p/C_{crea}), daily phosphate waste in urine (U-P), daily protein waste in urine (U-Pr) and minimal signs of Fanconi syndrome (FS; positive urine glucose and/or protein).
Results: Median age at time of diagnosis was 11.7 years. Median follow up from time of diagnosis was 1.2 months. Median dose of ifosfamide was 87 g/m^2. Median GFR decreased from 2.7ml/s to 2.2 ml/s ($p=0.001$). Median of S-crea was initially 48 μl/l and 58.1 μl/l at time of last follow up ($p<0.001$). Median of T_p/C_{crea} was 1.2 mmol/l and decreased to 1.1 mmol/l at the end of treatment ($p= 0.026$). U-P was initially and finally 11.9 mmol and 25.1mmol, respectively ($p = 0.008$). Median of tubular reabsorption of phosphate decreased from 95% initially to 90% ($p=0.001$). Daily waste of protein increased from 0.11 g to 0.43 g ($p= 0.051$). Minimal signs of FS developed in 9 of 17 patients (53%).
Conclsions: Patients with high cumulative doses of ifosfamide are at risk of renal impairement. Despite statistically significant differences of severeral measures observed in this study, clinical impact of post treatment values does not exceed grade 1 toxicity. Observation of minimal signs of FS developed in 53% of patients is of concern and further treatment of ES/PNET should be carefully focused on late effect too.

4.P.35

THE EFFECT OF PHYSICAL ACTIVITY PROMOTION ON DAILY PHYSICAL ACTIVITY IN PEDIATRIC BONE TUMOR PATIENTS: PRELIMINARY RESULTS

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Pediatric patients with lower extremity sarcoma often experience long lasting restrictions concerning physical activity and walking due to the required off-loading of the limb and other consequences of surgeries. Activity promotion during treatment in addition to physiotherapy could improve patients' activity levels and walking capabilities.
In the present study we investigated the ambulatory activity of 31 pediatric patients (13.7 ± 3.1 years, 1.63 ± 0.15 m, 51.9 ± 15 kg, 19.3 ± 3.7 kg/m^2) with Osteosarcoma or Ewing sarcoma at the lower limb using the StepWatch™ Activity monitor (SAM; Orthocare Innovations, USA). Sixteen patients regularly underwent supervised exercise interventions during inpatient stays, 15 did not receive any additional intervention. Step activities were measured for seven consecutive days during home stays at five different points in time, to determine a possible transfer of activity to everyday life.
Patients without intervention assembled considerably less steps than those in the intervention group. Before surgery they reached 25.4% of the intervention group (total n=16), six weeks after surgery 40% (total n= 8), after three months 46% (total n=10), after six months 72% (total n=13) and after one year 90%. However differences only reached significance at the first measurement.
Data presented must be considered as preliminary. Not all patients could be measured at all appointments due to impaired walking ability. Nevertheless activity promoting interventions during inpatient stays seem to have a positive influence on patients' daily walking activity. Though the differences between the groups are not significant they are considerable. Especially during treatment – as reflected by the first three measurements- patients could benefit from additional interventions exceeding typical therapy regimes. Interventions should be individualized to the patients' capabilities. Conclusions concerning tumor location or surgical procedures are not yet possible. Future research should furthermore concentrate on the effects of activity promotion on other fields of well-being.

4.P.36

EFFECTS OF AN EXERCISE INTERVENTION ON AREAL AND VOLUMETRIC BONE MINERAL DENSITY IN PEDIATRIC SARCOMA PATIENTS

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Several studies report a diminished BMD as a consequence of childhood cancer treatment. The aim of this study was to investigate the effects of an exercise intervention on BMD during treatment, since limited mobility is characteristic for cancer therapy and is a major determinant for bone loss.
We analysed DXA scans (Lunar Prodigy, GE Healthcare) of 53 patients (range 8 to 21 years at time of diagnosis) perioperatively (n=49), six (n=38) and twelve months (n=18) after surgery. Scans were performed for the established sites of the lumbar spine and both femora, as well as experimentally for both calcanei. Areal BMD was corrected to obtain volumetric BMD using the model of Kröger.
For both groups, areal and calculated volumetric BMD values were similar at the lumbar spine at time of surgery, as were the differences between affected and not affected femur and calcaneus. The six and twelve months postoperative measurements revealed higher volumetric and areal BMD at the lumbar spine for the intervention group, although significant differences were only found for volumetric BMD values six months postoperatively.
Furthermore, a comparison of both groups showed that the loss in bone density of the affected lower extremity was less pronounced for the intervention group: differences between affected and not affected femur were 9% to 73% higher in the femur and 20% to 29% higher in the calcaneus for the control group.
Previous reports dealing with diminished BMD in pediatric cancer patients were confirmed in this study. However, differences found in BMD between both groups indicate that an exercise intervention during treatment, consisting primarily of strength and endurance training, may inhibit bone loss in pediatric sarcoma patients. Furthermore, the calcaneal site may be an alternative when the determination of femur BMD is not feasible.

6.O.01

POTENTIAL CHEMOTHERAPY APPROACHES FOR ADVANCED ADULT TYPE SOFT TISSUE SARCOMA

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Soft tissue sarcomas (STS) include a spectrum of histologically and clinically different tumors. Patients are typically relatively young and the course of disease is characterized by early metastasis as well as limited response to chemotherapy. However, a few subtypes such as small round cell tumors (SRCTs) and rhabdomyosarcoma (except from pleomorphic), are considered chemotherapy-sensitive. In addition, reflecting successful translational research of recent years, gastrointestinal stromal tumor (GIST) and dermatofibrosarcoma protuberans have become model diseases for targeted oncological therapy. With a very limited number of active compounds at hand, treatment choices in metastatic STS with inkonsistent genomic alterations were easy to overview until only a few years ago. However, with novel therapeutic strategies such as the antiangiogenic approach and a multitude of novel compounds available both outside and within clinical studies, it may have become more difficult to keep track of currently available treatment options and their clinical safety and efficacy. Anthracyclines with or without ifosfamide are still considered standard of care in most STS-subtypes, especially in high-grade tumors. There is no evidence-based recommendation as to second-line treatment options. However, a number of established compounds, including dacarbazine/temozolomide, gemcitabine, taxanes, trofosfamide, DNA topoisomerase I inhibitors, DNA minor groove binders, and bendamustine, have shown activity. Recently, trabectedin, a DNA minor groove binder initially isolated from a sea sponge, has proven effective and received European approval for use in treatment-refractory STS. In addition, novel compounds such as bevacizumab, multityrosine kinase inhibitors, mTOR inhibitors, imatinib mesylate, and the thrombospondin agonist ABT 510 represent attractive partners for the above-mentioned cytostatic agents or may even be effective single agents in the clinically advanced setting. Novel combinations are being evaluated in clinical studies. In order to be successful, we may have to combine not only different compounds but also different targets beyond the proliferation machinery of sarcoma cells such as tumor angiogenesis, the tumor stromal compartment or tumor cell oncogene products.

6.O.02

PEDIATRIC SOFT TISSUE SARCOMA (STS) AS A MODEL FOR RARE TUMORS: HOW TO INTEGRATE CLINICAL RESEARCH INTO CLINICAL PRACTICE.

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While STS as a group represent a significant portion of all solid tumors in childhood, individual histologic entities are rare due to their extreme heterogeneity. This represents the principal obstacle to clinical trials. A compromise between clinical vs. statistical precision has been necessary in the majority of clinical trials on STS resulting in contradictory conclusions. Clinical trials have to reduce uncertainty but trials, which overlook clinical heterogeneity can even contribute to it. An example is many clinical trials, which have been carried out in the recent decades to answer the question of the role of adjuvant chemotherapy in “Non-RMS-STS”. Majority of these trials have overlooked clinically relevant subgroups. The result is that we still do not have certainty whether and which adjuvant chemotherapy is beneficial.
In addition, most clinical trials of treatments for STS rely on the endpoints of survival or event-free survival, so results have taken years to accrue and even longer to report. However, in STS with well defined genetic abnormalities and strong preclinical rationale for activity of a molecular targeted therapy the demonstration of clinical activity in only a few cases might be sufficient. In dermatofibrosarcoma protuberans, a very rare entity, the demonstration of clinical activity of the molecular targeted therapy was very convincing and led to approval of the drug, although the number of cases was very low.
International collaboration is necessary to obtain a sufficient number of patients but participation of many different centers with different expertise for a given rare tumor may compromise the quality of patient`s care. It is also difficult for many pediatric departments to open and maintain large numbers of trials with low accrual rates.
In conclusion, new methods for clinical research in the field of STS especially surrogate outcome variables and novel technique for early assessment of response are urgently needed.

6.O.03

NO INCREASE OF INCIDENCE RATES OF SOFT TISSUE SARCOMAS IN AUSTRIA - A POPULATION BASED EPIDEMIOLOGIC STUDY AND LITERATURE REVIEW

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Increasing incidence rates of soft tissue sarcomas (STS) have been reported. In the present study the authors have analysed the incidence of STS in Austria in a population-based study for the period 1984-2004 in comparison with seven international studies.
Age-adjusted incidence rates, gender- and age-predilection and geographic differences were analysed, comprising data from the Austrian National Cancer Registry, including all cases of STS in Austria between 1984 and 2004.
A total of 5333 cases was registered, male to female ratio was 0.8. The most common histotypes were sarcoma NOS (36%), leiomyosarcoma (24%), liposarcoma (12%), malignant fibrous histiocytoma (MFH) (9%) and fibrosarcoma (5%). Age-adjusted incidence rate was 2.4 per 100,000 per year. Analysis of annual incidence rates and three-year-periods showed no increasing trend (annual increasing gradient = -0.0025).
This study analysed the most recent data from a European population in comparison with seven other studies. An increase of incidence of STS as postulated elsewhere could not be confirmed. The incidence rate of STS in Austria (2.4 per 100 000 per year) ranges in the lower half of international incidence rates (1.8-5.0 per 100 000 per year). Different inclusion criteria (Kaposi´s sarcoma and dermatofibrosarcoma) and classifications in the various studies could be seen. These findings are more likely to cause the increase of incidence in some studies than true increase of STS due to new or accumulated risk factors.

6.O.04

PROGNOSTIC FACTORS AND OUTCOME FOR LOCALIZED EXTREMITY RHABDOMYOSARCOMA (RMS). THE RESULTS OF A POOLED ANALYSIS FROM US AND EUROPEAN COOPERATIVE GROUPS

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Objective: To determine patient characteristics and outcomes for extremity rhabdomyosarcoma (RMS) utilizing an international cohort of prospectively treated patients.
Methods: Data were collected from 566 patients (1984 through 2003) treated on cooperative protocols : US IRS III, IV Pilot, IV studies - SIOP 84, 89, 95 studies – Italian ICG 79, 88, 96 studies – German CWS81, 86, 91, 96 studies.
Results: 29 % of the patients were < 3 year old, 36 % were 3 to 10 year old and 35 % > 10 year old. 350 (63%) patients had alveolar RMS and 116 (22%) had regional nodes.
The overall survival and EFS were 65% and 51% at 5 years respectively and 59% and 48% at 10 years respectively.
By univariate analysis, EFS was influenced by age below 3 years but not by age over 10 years (EFS were 61%, 49% and 46% for patients below 3 years, from 3 to 10 and 10 years or more respectively). It was also influenced by tumor invasiveness, tumor size, lymph node involvement, histology, completeness of surgery at diagnosis and cooperative groups. In multivariate analysis of EFS, size, lymph nodes, quality of surgery, cooperative groups had independent impact. Age and histology had no more impact.
OS (univariate analysis) was influenced by age below 3 years but not by age over 10 years (OS were 77%, 61% and 58% for patients below 3 years, from 3 to 10 and 10 years or more respectively). In multivariate analysis, age, lymph nodes, tumour invasiveness, quality of surgery at diagnosis had independent impact. Histology, tumour size and cooperative groups had no more impact
Conclusion: This analysis shows that significant cut-point for age is 3 years, that histology per se has no impact on OS and EFS. It also underscores the impact of initial surgery on outcome.

6.O.05

THE IMPACT OF POOR RESPONSE TO INDUCTION CHEMOTHERAPY ON OUTCOME IN LOCALIZED EMBRYONAL RHABDOMYOSARCOMA – A REPORT FROM THE CWS STUDY GROUP

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Tumour volume reduction (i.e. response), assessed following induction chemotherapy, has been identified as a prognostic factor for localized embryonal rhabdomyosarcoma (RME) in the CWS studies. In combination with other risk factors, it has been used to stratify secondary local and systemic treatment. It is however unclear whether the poor outcome of non-responders is due to insufficient local and/or systemic post-induction treatment.
We analyzed post-induction therapy of RME-patients <21 years with unresected localized tumours (IRS-III) and poor response (NR, i.e. <33% tumour volume reduction) treated 1980-2005 in five consecutive CWS-trials. The NR were reviewed and subclassified (Objective Response (OR; i.e.<33%-0%) *vs*. Stable Disease/Progression (PD; i.e. no reduction)).
From 758 IRS-III RME-patients, 59 were NR (n=34 OR, n=25 PD). Induction for NR included dactinomycin, vincristine, alkylators ± anthracyclines in all patients. There were no significant differences in comparison of the control group and NR with regard to age, size, TN-classification, apart from site (p=0.04), and no differences regarding these parameters between OR and PD. Twenty-four NR received continued induction chemotherapy, n=32 other combinations, and n=3 no further chemotherapy following response assessment. Four patients were treated with additional high-dose chemotherapy. Fourty-two NR were irradiated with a median dose of 48Gy (control group: 45Gy). In 20 NR, the tumours were completely resected. As of 9/2008, with a median follow-up of 4.5 years (range: 0.9-12.1) for NR survivors, 34 NR are alive in CR. Reasons for the 25 deaths were: local/combined failure (n=21), systemic failure (n=1), and other reasons (n= 3). 5-yrs-OS was 71±4% for the control group, 78±15% for OR, but only 43±15% for PD (p<0.01).
Response is an important surrogate marker of outcome, but *per se* associated with a poor prognosis only in tumours without any volume regression to induction chemotherapy. Ineffective local control drives mortality in these patients.

6.O.06

COMPARING CHILDREN AND ADULTS WITH SYNOVIAL SARCOMA IN THE SURVEILLANCE, EPIDEMIOLOGY AND END RESULTS PROGRAM, 1983 TO 2005: AN ANALYSIS OF 1268 PATIENTS

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Synovial sarcoma (SS) is a typical soft tissue sarcoma subtype crosswise between the pediatric and the adult age groups. No published data describes a different biology of SS when arising in adults as opposed to children, but different therapeutic strategies have been developed for pediatric and adult oncology protocols dealing with SS (in particular concerning the use of systemic therapy) and different overall outcomes have been reported by pediatric and adult groups.
To better characterize the clinical features and outcomes of SS across the different age groups, we performed an analysis of all SS cases registered on the Surveillance, Epidemiology, and End Results (SEER) public-access database collected from various geographic areas in the United States, from 1983 to 2005.
We analysed 1268 cases, 213 children/adolescents (≤18 years) and 1,055 adults.
No major differences in stage distribution (localized, regional and distant stage) and clinical features were observed comparing the two age-groups, though a quite different pattern was recorded just for the small group of patients younger than 10 years (2.5% of cases, more extremity primaries, smaller tumors, mostly localized). The estimated 5-year cancer-specific survival was 83% for children/adolescents and 62% for adults ($p<0.001$). Female sex, non-black race, tumors located in the extremities, localized tumors and tumors <5 cm in size were associated with better survival. In multivariate analysis, adult patients had significantly higher mortality rates than children after adjusting for other variables.
In conclusion, our analysis showed that children/adolescents and adults with SS have a similar clinical presentation but a dissimilar outcome, suggesting that factors other than unfavorable clinical features might be involved in the unsatisfactory outcome of adult SS patients. It remains to be ascertained whether this difference may be related to biological variables or to historically-different treatment approach adopted in pediatric versus adult patients.

6.O.07

PROGNOSTIC VALUE OF PAX-FKHR FUSION STATUS IN ALVEOLAR RHABDOMYOSARCOMA: A REPORT FROM THE COOPERATIVE SOFT TISSUE SARCOMA STUDY GROUP (CWS)

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Alveolar Rhabdomyosarcoma (RMA) are characterised by chromosomal translocations fusing the PAX3 or PAX7 gene with FKHR in ~85%. Previous studies have suggested that PAX3/7-FKHR fusion types are related to prognosis. In order to prove these findings we performed a retrospective analysis of the PAX-FKHR fusion status and its relation to outcome in patients treated in the CWS trials.
Between 1986 and 2004, out of 446 RMA patients treated in four consecutive CWS trials (CWS-86, -91, -96 or -2002-P), tumor samples from 121 patients with adequate quality for analysis of PAX-FKHR fusion status by RT-nested PCR were available. Survival analysis depending on clinical risk factors and fusion status was performed using the Kaplan-Meier Method, the log rank test and the Cox regression model.
There were no major differences in distribution of known risk factors in the analysed cohort of 121 patients compared to all patients enrolled in the CWS trials. PAX-FKHR fusions were detected in 83%: 72 PAX3-, 29 PAX7-FKHR fusions. Patients with PAX3-FKHR positive tumors more often showed a pattern of adverse clinical risk factors (age >10 years, primary metastases, lymph node involvement) than the PAX7-FKHR positive group. The 5-year event free survival rate of patients with initially metastatic tumors positive for either of the two fusion transcripts was significantly lower compared with the fusion transcript negative cohort and the non-analysed RMA patients. There was no significant outcome difference between patients with PAX3-FKHR and PAX7-FKHR positive tumors in uni- and multivariate analysis.
In the present analysis, which is to our knowledge the largest reported so far, PAX-FKHR fusion type was no significant predictor for prognosis, thus not supporting results of previous studies.

6.O.08

TARGETING THE P53/HDM2 INTERACTION AS A THERAPEUTIC STRATEGY IN SYNOVIAL SARCOMA

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Mutations of the p53 gene are uncommon in synovial sarcoma, a high-grade tumor genetically characterized by the chromosomal translocation t:(X;18),that results in the fusion of SS18 with SSX gene.
We recently reported that SS18-SSX1 negatively regulates the stability of p53 by promoting its ubiquitination and degradation in a manner dependent on the ubiquitin ligase activity of HDM2. The negative effect of SS18-SSX1 expression on p53 was mediated by its ability to promote HDM2 stabilization through inhibition of HDM2 autoubiquitination. The final outcome translates into a deficient transactivation of p53-regulated genes: HDM2, PUMA,and NOXA that are important to preserve genomic integrity in response to cellular stress.
Our data uncovers a novel mechanism whereby, in synovial sarcoma cells with wild type p53, the SS18-SSX oncoprotein can negatively regulate p53 tumor-suppressive function by increasing the stability of its negative regulator HDM2.
We further hypothesise that chemical compounds that target the p53-HDM2 regulatory axis may rescue p53 function in synovial sarcoma. With this in mind we investigated the potential of the HDM2 antagonists, *nutlin-3* and of the recently discovered *tenovin 1*, to rescue p53 activity in synovial sarcoma cells lines. *Nutlin-3* effectively stabilized p53 half-life and trans-activating function, resulting in cell growth arrest and apoptosis.
We further observed that chemotherapeutic agents like doxorubicin also stabilized p53 in response to DNA damage but did not restore p53 transcriptional activity due to rapid complexing of p53 to HDM2. On the contrary, *nutlin-,3* stabilized p53 and inhibited p53-HDM2 interaction, thereby rescuing p53 tumor suppression function. Our results suggest that the inhibition of the p53-HDM2 interaction by small molecules is a highly potential therapeutic strategy for soft tissue sarcomas with wild type p53.

6.O.09

IDENTIFICATION OF TFE3 AND ASPL/TFE3 FUSION TRANSCRIPTS IN FORMALIN-FIXED, PARAFFIN EMBEDDED TISSUES IN ALVEOLAR SOFT PART SARCOMA (ASPS) - A POWERFUL DIAGNOSTIC TOOL

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Background: ASPS is a rare, high grade sarcoma primarily affecting children and young adults. Its origin remains enigmatic and there has until recently been no diagnostic markers. Diagnostic problems particularly occur when presenting as metastasis before detection of the primary tumour and when there is morphologic overlap with other malignancies. Recently, identification ASPS/TFE3 fusion transcripts and immuno-detection of TFE3 have been reported as useful diagnostic tools.
Design: 17 ASPS were analysed in terms of clinicopathologic characteristics, treatment and follow up. Archival formalin-fixed and paraffin embedded tissues were used for TFE3 immuno-histochemistry and RNA extraction followed by RT-PCR analysis and sequencing. Novel primers to detect ASPS/TFE3 fusion transcripts, type 1 and 2, were designed.
Results: The patients, 9 females/8 males, ranged in age from 3 to 46 years (median 23 years); 16 involved the extremities (9 lower, 7 upper) and one the pelvis. All but one patient had primary, curative surgery; chemotherapy and radiotherapy was given for metastatic disease. Five had lung metastases at diagnosis and 3 developed lung and brain metastases later. Four patients died of disease (after 1-5 years), 4 are alive with metastases and 9 are alive and well (after 6 mos.-10 years). 15/15 ASPS showed ASPL/TFE3 fusion transcripts (8 type 1, 7 type 2) and TFE3 immuno-positivity. Of 26 control tumours, several of which with overlapping morphologic features, none had fusion transcripts, 4 showed immuno-positivity (all granular cell tumours).
Conclusions: Immuno-detection of TFE3 and RT-PCR based identification of ASPL/TFE3 fusion transcripts in formalin-fixed/paraffin embedded tissues are powerful tools in the diagnosis of ASPS.

6.O.10

SPOT-SCANNING PROTON THERAPY OF SARCOMATOUS TUMOURS IN CHILDHOOD AT PSI

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Proton beam radiation (PT) is getting an increasing role in the treatment strategy of complex tumour cases and especially in children. AT PSI, over 100 children were treated so far.
In this analysis we present the evaluation of 62 children treated until the end of 2007 for sarcomatous tumours. Twenty-nine girls and 33 boys were included. Median age at time of diagnosis was 8.1 yrs. (range, 0.1-19.0). The histopathologies were embryonal RMS (n = 24), Chordoma (n = 10), Ewing sarcoma (n = 6), Chondrosarcoma (n = 5), unclassified/ undifferentiated RMS (n = 5), Osteosarcoma (n = 4) and miscellaneous. All, but 2 patients had localized disease at time of diagnosis. Tumour site was head and neck in 43 patients, and spine or pelvis in 19 patients. In 50 out of the 62 patients, PT was performed after biopsy or incomplete resection. Forty-four patients had received chemotherapy before or during PT. Median dose of irradiation was 54 Gy (range, 45 – 74 Gy) with 1.8-2.0 Gy fraction dose 4 - 5 times weekly.
Median FU time was 20 months (1.4 - 101). 54 children were still alive at the time of analysis. Twelve patients failed, of them 9 locally and 3 patients at distant site. Acute toxicity was exceeding grade 2 (RTOG/EORTC) mainly for bone marrow in children with parallel chemotherapy (n = 23). In 6 children skin/mucosal reaction was exceeding grade 2. Late effects were not exceeding grade 2 in the majority of children. One serious adverse event was observed in a very young girl with a parameningeal sarcoma experiencing a lethal ischemia in the pontine area after surgery, chemotherapy and PT.
In the vast majority of patients proton therapy was well tolerated. Local control and survival rates are promising. Longer follow-up time and a greater cohort will help to provide more reliable data.

6.O.11

PREVALENCE AND RISK FACTORS FOR INADEQUATE SURGICAL RESECTION OF SOFT TISSUE SARCOMAS

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Planning resection margins for soft tissue sarcomas is a compromise between functional sacrifice and therapeutic safety. In practice, the histological analysis of the resection margins often shows that the preoperative objective has not been achieved. We studied the prevalence and factors of risk of this surgical outcome.
This was a prospective monocentric study of 133 patients. The resection objectives, pathological results and operative reports were examined. Margins were classified according to the UICC (R0, R1, R2). Data were included in a grid which also included patient related and tumour related preoperative information. Inadequate resection was noted as planned R0 with R1 or R2 outcome. Statistical analysis was performed with Statview 5.0.
The prevalence of inadequate resection was 25.2%. Among the factors analysed, the aspect of tumor limits (badely or well defined) was significantly related to poor surgical results (odds ration 2.85 [1.47-5.52], $p < 0.005$). No other significant risk factor could be identified. Margins greater than two mm were associated with adequate surgery in every case.
No preoperative risk factor predictive of inadequate resection margins was clearly identified in this study. Postoperatively, the microscopic aspect of the proliferation limits at the final pathology examination is for us significantly associated with inadequate resection. However the current classification for resection margins lacks precision, especially regarding R0 and R1 when margins are small, in defining the risk of inadequate resection. This appears to be the source of the difficulties encountered in interpreting pathology samples and therefore in choosing the right treatment. Further follow-up is needed to clarify such questions.
We conclude that where resection margins are thin (less than two mm), the definition of R0 or R1 resections should be clarified to optimize patient care. To achieve this, potential risk factors for inadequate resection such as tumor limits should be taken into account and further studied.

6.P.01

MOLECULAR TYPING FROM ARCHIVAL PARAFFIN-EMBEDDED SYNOVIAL SARCOMAS

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Synovial sarcomas are mesenchimal tumours with undefined histogenesis which represent 5-10% of soft tissues tumours; they are divided into different subtypes according to morphology and epithelial differentiation. From a molecular point of view, synovial sarcoma is characterized by t(X;18)(p11;q11) translocation which joins SYT gene with a member of SSX gene family. We developed an efficient method to detect the two main fusion transcripts SYT-SSX1 and SYT-SSX2 based on RT-PCR or Real-Time PCR applied to archival paraffine-embedded samples.
This study includes 49 patients surgically treated for synovial sarcoma and analyzed with routine immunohistochemical analysis. We used alternatively nested-PCR or Real-Time PCR, with SYBR green method, to detect SYT-SSX transcripts: these techniques allowed us to discriminate between the two transcripts.
In 42 subjects out of 49 we could find a specific fusion transcript and, in particular, 31 patients were carriers of SYT-SSX1 translocation. Interestingly we could find 6 patients who were carriers of both SYT-SSX1 and SYT-SSX2 transcripts. We selected nine samples for Real-Time PCR analysis and we could quantify the reciprocal ratio between the two fusion transcripts when they were both present in the same sample.
The use of molecular techniques such as RT-PCR represents a sensitive and reliable tool as a support to histopathologic diagnosis of synovial sarcoma. Moreover, Real-Time PCR enormously enhances sensibility and enables to determine single transcript quantity when both SYT-SSX1 and SYT-SSX2 are present in the same sample. This method can also be used to reclassify those cases whose diagnosis is still undefined after routine analysis.

6.P.02

SYNOVIAL SARCOMA OF CHILDHOOD – SURGICAL LESSONS

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Synovial sarcoma (SS) of childhood is considered chemoresponsive, what frequently leads to conservative surgical approach.
Aim of the report is to assess whether that approach is sufficient and what are other clinical factors influencing the outcome.
Patients: 23 children (aged 3 months - 17 years) treated in 5 cooperating centres for nonmetastatic SS located in the limbs(Fu>36 months). Treatment: primary or secondary resections, chemotherapy and radiotherapy (in case of resection R1 or R2 or relapse). Locations of tumours: thigh/6, shank/1, popliteal fossa/4, cubital fossa/3, axilla/2, forearm/2, foot/3, arm/1, hand/1. Primary R0 achieved in 3, R1/5, R2/3. Twelve after initial biopsy and 3 after primary R2 were submitted to chemotherapy and secondary surgery. 12/15 those resections were R0, 3/15 R1. Two of them underwent mutilating resections.
Results: 11 pts are in CR. 12 relapsed (7 local, 5 metastatic). Initial locations of the relapsing tumours were around joints/4, foot/hand 4, thigh 3, arm 1. Seven of them died despite aggressive re-treatment, 2 are alive with disease, 3 are in second CR. Quality of resections (primary or secondary) in 7 locally relapsing pts were R0 in 3, R1 in 3 and biopsy only /1 (CR after CHT alone, refused local treatment). Of 2 submitted to mutilating resections, 1 relapsed in the lungs (2nd CR after re-treatment and metastasectomy).
Summary:

1. R0 doesn‘t prevent from local relapse (3 of 7 pts relapsed after R0 vs 4/7 with R1).
2. Mutilating resections (amputations) were unfrequent (2) and were not followed by local relapses. One metastatic relapse occurred and was finally cured.
3. Locations at risk seemed joints and distal parts of limbs (8/12 of the relapsing pts).
4. Relapsed implied weak chance for long-term second CR (3/12).

6.P.03

HIGH-RISK SYNOVIAL SARCOMA OF CHILDREN TREATED WITH INTENSIVE CHEMOTHERAPY, SURGERY AND RADIATION THERAPY

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Synovial sarcoma is the most common NRSTS, that typically affects the extremities of adolescents. To improve the results of the treatment of synovial sarcoma for children and adolescents is the target of this study. 19 children and adolescents at the mean age of 10,84±3,28 years (9 males, 10 females) with synovial sarcoma were treated between 1999 and 2008 years at the Research Institution of Pediatric Oncology in the Russian Cancer Center. Histologically, 5 patients had the biphasic,12 had the monophasic, and 2 of them had the poorly differentiated pattern. The most often affected area was the area of the lower extremity - 10 cases, the area of the upper extremity was affected in 3 cases, and the trunk – 6 cases. According to the staging systems adopted, the size >5cm (TB) was reported in 12 cases. Five patients (non-staging) had relapse of disease. Four patients had nodal involvement, and 4 had distant metastases (mostly at lungs).
The general scheme of the treatment included: 8 courses of chemotherapy (used ifosfamide or cyclophosphamide, ethoposide, carboplatine); the harvesting and preservation of the stem cells after the stimulation of the haemophoesis by G-CSF, the stage of the local control of the tumor consisting of the surgical ablation of the primary lesion (in 1 case it was not available) and the radiotherapy of the initial tumor and metastasis left after the induction.
The partial effect was registered by most of the patients – 80%. We observed 1 case of progression of the disease during inductive CT. The toxicity of intensive chemotherapy was reduced by support of subtransplantation doses of peripheral blood stem cells - 0,9-1,5±0,1·106 per kg. In our research we have analyzed the 5-year overall and disease free survival. Thus, 5-year disease-free survival was 66,1±11,3 %, overall 5-year survival –75,6±10,6%.

6.P.04

ANALYSIS OF STERNOTOMY AS TREATMENT OPTION FOR THE RESECTION OF BILATERAL PULMONARY METASTASES IN PEDIATRC SOLID TUMORS

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Radical surgical resection of metastases is an important prognostic factor for survival of patients suffering from solid pediatric tumors. The aim of this study is to evaluate the efficacy of median sternotomy as treatment option for the resection of multiple bilateral lung metastases in children with different tumor entities. Furthermore, the sensitivity of preoperative imaging (CT) was assessed by intraoperative findings.
Between 2002 and 2007, thirteen children (4x sarcoma, 4x nephroblastoma, 5x hepatoblastoma) underwent median sternotomy for resection of bilateral lung metastases after R0 – resection of the primary tumor. In 6/13 cases, the sternotomy was combined with the primary tumor reseMedian patients` at the first operation age was 5 years (range: 11 months – 17 years). The median total number of resected metastases per operation was 9 and ranged from 0 to 65. In 13/16 operations, the intra-operative number of metastases did not agree with the preoperative radiological work-up. Median hospital stay was 14 days (range from 9 to 36 days). 10/13 children are alive after a median follow–up of 13 months (range from 6 to 66 months).
Median sternotomy is an adequate treatment modality for the resection of bilateral pulmonary metastases as a one stage procedure. The combination of primary tumor resection with sternotomy should be considered as treatment option. Complete resection of metastases of solid pediatric tumors should be aimed for in order to increase the survival of these patients.

6.P.05

IRRADADIATION IN SOFT TISSUE SARCOMA: PREOP OR POSTOP?

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Local control cannot be achieved in many cases of soft tissue sarcoma by surgery alone. Additional irradiation is often necessary. This reveals the question of the optimal sequence of resection, reconstruction and irradiation.
Material: We present
1.) A review of the literature concerning preop and postop irradiation in soft tissue sarcoma.
2.) The criteria of decision making in 15 cases of our own patients concerning the question of preop and postop irratdiation.
Results:
1.) Review of the literature:
There ist a certain benefit in additional irradiation concerning local control, but there is no evidence in favour of preop or postop irradiation concerning overall survival.
Clinical cases:
- Preop irradiation is preferred in all cases of microvascular bone repair in order not to interfere with bony healing and hypertrophy of the transplants.
- Pathological fractures after irradiation are very difficult to treat.
- In children irradiation has to respect the epiphyseal areas.
- Microvascular tissue transfer after irradiation may fill up big tissue defects after wide resection, may improve wound healing and prevent lymph edema

6.P.07

LONG TERM SURVIVAL OF CONGENITAL FIBROSARCOMA, ABOUT 3 CASES

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Congenital fibrosarcoma (CFS) is a rare tumor most often affecting extremities of babies. Considering age, surgery of primary is preferred . Nevertheless amputation rate remains high. Preoperative chemotherapy (CT) role must be emphasised . We present 3 cases receiving preoperative CT.
Patients and methods in 1985 , we treated a 3 months old girl for CFS of the thigh. To avoid amputation, preoperative CT (3 Ifosfamide- Vincristine- Actinomycine D) was performed leading to complete radiological and histological response. She benefited of conservative surgery She is in first complete remission 23 years later .
In September 1999, a 3 ½ y old boy with recurrent l buttock CFS operated elsewhere twice (6 months old , 2 years old) , received preoperative chemotherapy with good clinical and radiological response. “En-bloc” extra tumoral resection was performed. Histology showed viable tumoral cells . We completed treatment by chemotherapy. In 01/ 2003 bilateral pulmonary metastases occurred leading to surgery and chemotherapy. In 09/ 2003 a new local recurrence appeared treated by surgery and post-operative chemotherapy. From this time, he received Alpha interferon. He is in complete remission for 6 years.
In 12/ 2005, a 14 y old girl, with local recurrence of CFS, treated elsewhere at the age of 5 months by partial surgery and chemotherapy (remained in remission for 13 years)was admitted . Since this time, she recurred locally despite resections and multiple lines of chemotherapy, but without metastasising. She was amputated in 2008.
Conclusion: preoperative chemotherapy is feasible despite low age of the patients, can allow conservative surgery and avoid late metastases.

6.P.08

CONGENITAL INFANTILE FIBROSARCOMA (CIFS) OF THE FOREARM: A CASE REPORT

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Congenital infantile fibrosarcomas (CIFS) is a rare tumor of childhood that can be diagnosed from birth to 15 years. It has a ratio of 3.74/100 000 children and is well defined nosological entity with a well-defined pathogenetic patterns: translocation (12, 15) (p13, q25) with fusion of the gene ETV6-NTRK3.
The differential diagnosis of upper CIFS in infants must be made with lymphatic malformations, and when associated with the Kasabach-Merritt phenomenon's (disseminated intravascular coagulopathy), haemangiomas, emangioendotelioma kaposiforme. In 26% of cases is congenital, while in 63% is diagnosed in the first 5 years. Unlike fibrosarcomas of the adult is characterized by a low rate of metastasis and a high survival rate (90% at 5 years). 74% of cases is observed in the limbs (upper> lower, distal>proximal).
The treatment of choice should to be, where possible, limb salvage and the recurrences are variable between 17% and 43%.
The purpose of this paper is to present a case of CIFS, the clinical features, the oncological treatment, the reconstructive solutions and functional results obtained after reconstruction.
Case report.
The child (Z.A. female), was diagnosed with a neoplasia of soft tissues of the right forearm before birth.
At birth the child underwent a needle biopsy with a diagnosis of CIFS.
The patient received four cycles of chemotherapy with reduction tumor mass of more than 50% of volume.
At month four she underwent an exeresi with wide margings and sacrifice of the radial nerve.
The reconstruction required a free flap of re-innervated latissimus dorsi muscle. After 30 months from the surgical procedure the child is disease free and has recovered extesion of the muscles of the hand and fingers.

6.P.09

HEAD AND NECK SOFT TISSUE SARCOMAS IN CHILDREN AND ADOLESCENTS. EXPERIENCE FROM ONE INSTITUTION

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Beckground: Head and neck region is a rare site location for sarcomas and there are difficulties of surgery management .With the exception of those arising in relatively superficial locations, are rarely amenable to wide local excision. Incisional biopsy for diagnostic purposes is usually all that is feasible. Multimodal treatment is mandatory to achieve local control.
The present study examines multimodal treatment outcome in children and adolescents with head and neck soft tissue sarcomas (H&NS).
Patients and Methods. Patients with H&NS who underwent chemotherapy +/- radiotherapy, after surgery, in Institute of Oncology Bucharest between 1990- 2007 were identified. Clinical charts and pathology reports were examinated.
The study included 42 pts.(29 male and 13 female); median age was 14 years years (range 3 – 21) Sites of primary tumor: parameningeal: 18 pts; nonparameningeal 16 pts and orbit: 8pts.
Histologic types: rhabdomyosarcomas and undifferentiated sarcomas represent 52% . Staging (TNM pretreatment staging classification for IRS-IV): St. I+II-36% ; St. III- 34%; St.IV-30%
All the pts were treated multidisciplinary: Surgery + Chemotherapy(PCT) +/- Radiotherapy(RT). Type of surgery performed: partial excision:54%; complete excision: 4 pts (9%); incisional biopsy: 37%. Type of RT: Exclusive RT in inoperable tumors(4 pts) ; external RT- postoperative(59%) curietherapy: 1 pt; gammaknife: 1pt. Neoadjuvant PCT were applied for 16% of pts and adjuvant PCT for 85,7% of pts. . Chemotherapy protocols used after 1992 was: IVA, IVE, VAIA, CEVAIE, and before 1992: CYVADIC, CYVADACT. All cases were followed minimum 2 years after the end of the treatment.
Results: Overall survival estimated by Kaplan Meier curve: 66%/ 1 year, 43%/ 5 years. OS according to the stages of disease ; stage I-II: 93% at 1 year,73% ar 5 years; stage III and IV: 47% at 1 year, 23% at 5 years.
EFS in sarcomas treated with S+PCT+RT is 41%, versus 16.5% for sarcomas treated with S+CT.
Observations: The diagnosis in advanced stages was due to the confusion with nononcological diseases.
Conclusions. 1. EFS was highest in sarcomas treated S+CT+RT face to sarcomas trated S+CT. 2 EFS at 2-3 yrs. in children‘s soft tissues sarcoma could be considered as cure.

6.P.10

LIPOSARCOMA IN CHILDREN AND ADOLESCENTS: AN ANALYSIS OF PROSPECTIVELY COLLECTED MULTICENTRIC DATA IN THE FRAMEWORK OF THE CWS STUDY GROUP

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Liposarcoma (LPS) is among the most common soft tissue sarcoma (STS) in adults, accounting for >10% of all STS. In children and adolescents, however, LPS are a rarity. Limited data about best treatment of pediatric LPS are derived from the scarce single-centre reports encompassing no more than a dozen patients.
Between 10/1980-6/2008, 18 of >3,500 patients <19 years with sufficient clinical data registered with CWS in Germany and Poland had a first diagnosis of LPS confirmed by reference pathologic review.
Median age was 14 years, median follow-up for survivors as of 2/2009 seven years. Sixteen patients had localized, two metastatic LPS at diagnosis. Lymph-nodes were affected in a single case. The most frequent primary site were the limbs (n=11), the remaining seven were trunk tumours (abdomen n=4, thorax n=3). 10/18 primary tumours were >5cm. Thirteen LPS were completely resected at best surgery, and microscopically residual disease remained in two more tumours. Six individuals received radiation with a median dose of 45Gy, including one of the two R1-resected patients. Nine patients received multiagent chemotherapy (only two of them since 1996 onwards). Response to induction treatment could be assessed in three of these nine individuals, but tumour volume regression occured in a single case only. Four patients died of disease, among them two of the three patients who did not achieve a CR with primary treatment. Two relapses (one combined, one metastatic), both involving the lungs, occurred one years after diagnosis and these patients were not salvaged. Actuarial 5-year EFS and OS survival rates were 69±23 and 81±20%, respectively.
LPS account for <0.1% of childhood STS. The golden standard of treatment and key to cure is complete surgical excision. The role of radiation and/or chemotherapy remains unclear, but both modalities do not appear to be indicated in completely resected, localized tumours.

6.P.11

COMBINED TREATMENT OF MALIGNANT FIBROUS HISTIOCYTOMA IN CHILDREN

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The purpose of the our study was to analyze prognostic factors characterizing biological behaviour of a tumour and specific features of the patient and to develop rational strategy of the combined treatment of malignant fibrous histiocytoma (MFH) in children.
Between 1982 and 2008 fifty patients with MFH were observed and treated in our center. 24 (48%) were male and 26 (52%) were female. In all cases the diagnosis was confirmed by histological examination. We use polychemotherapy consist of alternating courses of CDDP, adriamicin, ifosfamide and etoposide and high-dose methotrexate (8-12 g/m²). Intensive polychemotherapy allow us to expand indications for limb salvage treatment. Using growing (conventional and non-invasive types) endoprostesis improved the quality of life. 2-years RFS was 80,9±8,5% and 5-years RFS was 70,4±10,1% (Kaplan-Meier curves, p=0.03). The most significant prognostic factors were grade of histological response and type of polychemotherapy (conventional or intensive).

6.P.12

TREATMENT RESULTS OF PEDIATRIC NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMAS

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The nonrhabdomyosarcoma soft tissue sarcomas constitute a heterogenous group of rare mesenchymal tumors that account for less than %5 of pediatric cancers. Their biology and optimal treatment is not well understood. This study retrospectively analyses a small subset of surgically treated patients.
Fifteen patients with a mean age of 11.4 years (4 months – 16 years) were followed-up for a mean of 48 (2-124) months. The histologic diagnosis was synovial sarcoma in 5 patients; soft tissue Ewing Sarcoma in 3; fusiform cell sarcoma in 3; malignant peripheral nerve sheath tumor in 2; fibromyxoid sarcoma in 1 and myxoid liposarcoma in 1. The tumor was located in the upper extremity in 6 patients; thigh in 4; inguinal region in 2, foot in 2 and gluteal region in 1. Eight patients received preoperative chemotherapy and 5 received preoperative radiotherapy. Two patients had pulmonary metastasis at the time of admission. Thirteen patients were operated by limb salvage procedures and 2 underwent amputation.
Tumor resection was radical in 2 patients, wide in 12 and marginal in 1. Five patients received adjuvant chemotherapy and 5 received adjuvant radiotherapy. There were 5 local recurrences after 23.8 (14-40) months; three patients underwent wide resection for recurrence and two received chemotherapy and radiotherapy. Three patients had systemic metastases after a mean of 32.3 (27-40) months. There were no major complications but local wound problems were encountered. Three patients died of disease after a mean of 65.3 months (32-124 months). Two patients had metastatic disease and 10 had no evidence of disease in the last follow-up visit.
Pediatric soft tissue sarcomas can be treated following the principles of adult soft tissue sarcomas, except for wide utilization of radiotherapy in neoadjuvant and adjuvant setting. Treatment results are similar to adult patients.

6.P.13

THE ANALYSIS OF FACTORS PREDICTING SURVIVAL IN CHILDHOOD MALIGNANT AND INTERMEDIATE VASCULAR TUMOURS. THE RETROSPECTIVE COOPERATIVE STUDY OF THE POLISH AND GERMAN PAEDIATRIC SOFT TISSUE SARCOMA STUDY GROUPS

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Objective: providing the rarity of malignant and intermediate vascular tumours (MVTs, IVTs) in children little is known about their clinical course, optimal treatment and variables predicting survival.
Material and methods: 32 children with MIVTs (14 angiosarcomas-AS, 5 epithelioid haemangioendotheliomas-EHE and 13 IVTs), registered in Polish and German Paediatric Soft Tissue Sarcomas (STS) Study Groups, treated with CWS-81, -86, -91 and -96 protocols.
Results: AS presented with advanced disease (84%), deep-seated T2 invasive tumours (71%), >5cm in diameter (64%). Primary excision (PE) was incomplete in all and response to CHT/RTX disappointing. Nine/14 children entered CR; however all relapsed and, except one, died of disease. EHE and IVTs presented mainly in local stages (66,7%) and tumours >5cm (72%). Complete PE was feasible in 30% and response to CHT/IFN poor in half. 16 patients entered CR, but six relapsed and, except one, died of disease.
In multivariate analysis male gender, AS histology, tumour size >5cm, T2 invasiveness and lack of CR after Ist line therapy were independent predictors of poorer 5-year-OS, while AS histology and T2 invasiveness – of inferior 5-year-EFS. Radicality of PE was an independent prognostic factor for survival in univariate but not multivariate analysis.
Conclusions:
1. Current WHO classification has placed EHE in MVTs, however it may behave similarly rather to IVTs than AS.
2. Male gender, AS histology, tumour size >5cm, T2 invasiveness and lack of remission after Ist line therapy were independent predictors of inferior 5-year-OS while AS histology and T2 invasiveness – of inferior 5-year-EFS.
3. In contrast to most studies, radicality of PE was not an independent prognostic factor for survival.
4. High rate of patients not responding to classic CHT and developing metastatic recurrences suggests an urgent need for modification of systemic therapy.
5. Problem of efficient therapy of childhood AS is the most appalling.

6.P.14

CORRELATION OF PROLIFERATION INDEX KI67 WITH GRADE AND RECURRENCE TYPE OF SOFT TISSUE SARCOMAS

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Analysis of correlation of proliferation index Ki67 with grade and recurrence type of soft tissue sarcomas.
We reviewed 34 patients treated in RCRC RAMS. 53% patients were female, 47% – male. Adult patients – 97%, children – 3%. Soft tissue tumors localized on lower extremities in 47% cases (hip, shank), on upper extremities in 20% cases (shoulder, forearm, hand), on trunk in 24% cases, on head and neck in 9% patients. Histological subtypes were monophase synovial sarcoma – 32%, malignant fibrous histiocytoma – 23%, liposarcoma – 18%, malignant shwannoma – 6%, and other types in isolated instances. Synovial sarcoma more often observed in young and middle age women, malignant fibrous histiocytoma – in old men, liposarcoma – equally often in middle and old men and women. We observed soft tissue sarcoma grade 2 (FNCLCC) more frequently. Local recurrence development in 35% cases, number of recurrences was from 1 to 6. Distant metastases were in 8 patients (in lungs, lymph nodes, bones). We used monoclonal antibody Ki67 (clone MIB-1). Proliferation index Ki67 evaluated in the following way: low level - <25% of tumor cells, middle level – 25-50%, and high level - >50% of tumor cells.
1. Proliferation activity Ki67 increase in cases with high grade soft tissue sarcoma (in grade 1 tumors – low and middle proliferation activity, in grade 2 tumors – middle and high proliferation activity, in grade 3 tumors – only high proliferation activity). 2. Proliferation activity Ki67 increase in recurrent tumors (2-3 times more in comparison with primary tumors). 3. In cases with low level of proliferation index Ki67 were observed more number of local recurrences (>3), and long interval to distant metastases. If level of Ki67 was high, time interval to local recurrence was short, number of local recurrences <3, lethal outcome occurred often.

7.O.01

PROTON AND CHARGED PARTICLE RADIOTHERAPY FOR CHALLENGING SARCOMAS OF BONE AND SOFT TISSUES

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Background: Bone sarcomas are rare primary tumors. Radiation therapy (RT) can be useful in securing local control in cases where negative surgical margins cannot be obtained or where tumors are not resected. Recent technical advances in RT offer the opportunity to deliver radiation to these tumors with greater precision and accuracy, thus allowing higher doses to the tumor target with less dose to critical normal tissues, which can improve local tumor control and/or reduce treatment-related morbidity. Results of a recently published prospective trial of patients with spine sarcoma treated with high dose photon/proton radiation +/- surgery +/- chemotherapy will be presented to illustrate these concepts.
Methods: Methods and Materials: Eligible patients had nonmetastatic, thoracic, lumbar, and/or sacral spine/paraspinal sarcomas. Treatment included pre- and/or postoperative photon/proton XRT with or without radical resection; patients with osteosarcoma and Ewing's sarcoma received chemotherapy. Shrinking fields delivered 50.4 cobalt Gray equivalent (Gy RBE) to subclinical disease, 70.2 Gy RBE to microscopic disease in the tumor bed, and 77.4 Gy RBE to gross disease at 1.8 Gy RBE qd. Doses were reduced for radiosensitive histologies, cochemoradiation, or when diabetes or autoimmune disease present. Spinal cord dose was limited to 63/54 Gy RBE to surface/center. Intraoperative boost doses of 7.5 to 10 Gy could be given by dural plaque.
Results: A total of 50 patients (29 chordoma, 14 chondrosarcoma, 7 other) underwent gross total ($n = 25$) or subtotal ($n = 12$) resection or biopsy ($n = 13$). With 48 month median follow-up, 5-year actuarial local control, recurrence- free survival, and overall survival are: 78%, 63%, and 87% respectively. Two of 36 (5.6%) patients treated for primary versus 7/14 (50%) for recurrent tumor developed local recurrence ($p < 0.001$). Five patients developed late radiation-associated complications; no myelopathy developed but three sacral neuropathies appeared after 77.12 to 77.4 Gy RBE.
Conclusions: Local control with this treatment is high in patients radiated at the time of primary presentation. Spinal cord dose constraints appear to be safe. Sacral nerves receiving 77.12-77.4 Gy RBE are at risk for late toxicity. Similar approaches may be considered for other challenging bone and soft tissue sarcomas.

7.O.02

KINOME PROFILING OF CHONDROSARCOMA REVEALS SRC-PATHWAY ACTIVITY AND DASATINIB AS OPTION FOR TREATMENT

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Chondrosarcomas are notorious for their resistance to conventional chemo- and radiotherapy, indicating there are no curative treatment possibilities for patients with inoperable or metastatic disease. We therefore explored the existence of molecular targets for systemic treatment of chondrosarcoma using kinome profiling.
Peptide array was performed for 4 chondrosarcoma cell lines and 9 primary chondrosarcoma cultures. Acitivity of kinases was verified using immunoblot and active Src- and PDGFR signaling were further explored using imatinib and dasatinib on chondrosarcoma cell lines and primary cultures.
The AKT1/GSK3B pathway was clearly active in chondrosarcoma. In addition, the PDGFR pathway and the Src kinase family were active. PDGFR and Src kinases can be inhibited by imatinib and dasatinib, respectively. While imatinib did not show any effect on chondrosarcoma cell cultures, dasatinib showed a decrease in cell viability at nanomolar concentrations in 3 out of 5 chondrosarcoma cultures. Whereas inhibition of phosphorylated Src (Y419) was found both in responsive and non-responsive cells, caspase-3 related apoptosis was found only in cell line GIST882, suggesting that the mechanism of decreased cell viability in chondrosarcoma by dasatinib is caspase-3 independent.
In conclusion, using kinome profiling we found the Src pathway to be active in chondrosarcoma. Moreover, in the chondrosarcoma cell lines and primary cultures we showed that the inhibitor of the Src pathway, dasatinib, may provide a potential therapeutic benefit for chondrosarcoma patients which are not eligible for surgery.

7.O.03

RISK PROFILING FOR BONE METASTASIS AND BREAST CANCER: THE INFLUENCE OF THE 1498 C/T POLYMORPHISM OF THE VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF)

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Introduction: Breast cancer is the most frequently diagnosed cancer in western countries and bone metastases of breast cancer cause significant morbidity. Tumor growth and progression requires the formation of new blood vessels, a process called angiogenesis. Angiogenesis is a complex multifactorial process involving a variety of proangiogenic and proteolytic enzyme activators and inhibitors. The most important regulator of angiogenesis is vascular endothelial growth factor (VEGF), which is overexpressed in several tumor tissues. The single nucleotide polymorphism 1498 C/T of VEGF was associated with increased plasma levels of VEGF. In this case controlled study, we analyzed the role of this polymorphism in bone metastasis of breast cancer.

Material and Methods: We genotyped 839 female breast cancer patients. The study was performed according to the Austrian Gene Technology Act and has been approved by the Ethical Committee of the Medical University Graz. According to breast cancer staging, patients were divided in three groups, representing patients without metastases (n = 708), those with metastases other than bone (n = 69), and those with bone metastasis (n = 62). Results: Frequency of the 1498 CC genotype of VEGF was significantly lower among patients with bone metastases (6.5%) than among those with other metastases (23.2%; p=0.005) or no metastases (23.4%; p=0.002). Odds ratio of the CC genotype for bone metastases was 0.22 (95% CI 0.08 - 0.61; p = 0.004). Conclusion: We conclude that the homozygous 1498 C genotype of VEGF may be protective against development of bone metastasis in breast cancer patients.

7.O.04

EXPRESSION ARRAY ANALYSIS OF OSTEOSARCOMA CELL LINES TO DETERMINE CANDIDATE GENES FOR INVASIVENESS

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Osteosarcoma (OS) is the most common primary malignancy of bone, with up to 80% of patients suffering from metastatic or micrometastatic disease at the time of diagnosis. For the metastatic potential of tumours invasiveness plays an important role. This study intends to determine new candidate genes for cell invasiveness.
Eight OS cell lines (MNNG, HOS, MG63, SJSA1, OST, ZK58, U2OS, SAOS) were analysed using a modified Boyden Chamber Assay to separate invasive and non-invasive cells. Total RNA isolation and Illumina hybridisation Arrays (V3 bead arrays) were performed for both fractions.
Out of the eight cell lines, five (MNNG, HOS, MG63, SJSA1, OST) displayed an invasive fraction between 1.76 and 0.02%, which proved sufficient for subsequent RNA analysis. Pair wise comparison yielded 161 differently expressed genes between invasive and non-invasive cells. These are involved in important pathways such as cell motility, cell communication or signal transduction.
The generated new candidate genes might play an important role in metastasis of OS. Their functional characterization has been started combining knock-down experiments (RNAi) with the invasion assay. Validation will be done by RT-PCR and immunohistochemistry on a larger sample using OS-TMAs. Determined genes and pathways will be correlated with clinical parameters like metastasis, survival and chemotherapy sensitivity in order to improve understanding of the biology of OS.

7.O.05

WHERE IS THE LIMIT OF SILVER-COATINGS AS TOXIC AGENT AGAINST EARLY AND LATE INFECTIONS IN MEGAENDOPROSTHESIS?

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Infections are the most uneventfull complications after tumor resection and implantation of a maegaendoprosthesis.Silver-coating of megaendoprosthesis has become a regular procedure in our department since last year in tumor cases. Especially in revision cases with high risk of infection they play a major role in preventing adhesion of bacteria. The successful reduction in infection rates show the effectiveness of the coating but still leave the question “how much coating do we need?” and “how much coating can be tolerated.
Latest research concentrated on the coating of the stems, since they can still be the source of the infection if everything else is coated by silver already.
Summarised so far, our experience in a rabbit model, a phase I Trial in humans and prelimnary results in Phase II Trials in humans showed no toxic side effects.
Driven so far it seems to be sensible to extent the silver coating. So far, the coating is limited to all areas without joint movement or bone contact. An Animal trial was performed anylising the osteointegrative properties of an silver-coated stem versus an regular Titanium stem in 17 dogs. After 12 months of regular X-Ray Analysis a Pull-out test and a concentration analysis has been done.
Results showed high significantly ($p<0.001$) an osteointegration in 8 out of 8 titanium stems with an average pull-out force of 3764 Newton (Range 1755- 5967 Newton). Silver-coated stems showed no signs of Osteointegration in all 9 out of 9 femurs. The average pull-out force was 21 Newton (Range 0- 186 Newton). A cemented control could resist a pull out force of 350 Newton. Analysis of the silver concentration directly in the first millimeter of the bone-implant interface and the second millimeter showed highly elevated silver levels.
The silver concentration in the bone-implant interface at Titanium stems ranged from 0.3 to 3502 parts per Billion (ng/g) compared to silver-coated stems ranging from
303 to 2.418.800 ppb parts per Billion (ng/g).
Discussion: Sharing the histologic picture and reactions of the osteoblasts to the silver-coating there are several possible reasons for failed osteointegration. We want o discuss wether these has to be considered as a toxic response or just an adverse reaction.
In summary, surgeons have to decide in the future how much silver they need in each individual case concerning intramedullary infection prophylaxis. The balance between loosening or infection should be based on long term expectations, taking into account that even after successful resection of a tumor an ongoning infection can lead to loosening of a limb or even life. Apart from intramedullary use, we recommend silver as a safe adjuvant therapy in all suited patients undergoing endoprosthetic reconstruction after tumor resection.

7.O.06

METABOLIC CHARACTERIZATION WITH (18F)FDG-PET/CT OF LUNG NODULES IN PEDIATRIC OSTEOSARCOMA (OS) AND EWING'S SARCOMA (ES) PATIENTS

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PET/CT is successfully used in metabolic characterization of lung nodules in adult patients. An SUV max of 2.5 is generally accepted to distinguish benign from malignant lesions; for small solitary lung nodules some authors recommend visual evaluation rather than only SUV, suggesting that classical SUV criterion of 2.5 is inappropriate.
In pediatric patients interpretation of nodular opacity is still a clinical problem: specificity of CT in a pulmonary nodule, especially when small, is still limited.
Aim of this prospective study was to evaluate PET/CT for non invasive characterization of pulmonary nodules in pediatric bone sarcomas.
Materials and methods: 56 whole-body PET-CT exams were performed in 19 patients with OS (14 female, 5 male) and 9 with ES (4 female and 5 male); median age at the first PET/CT exam was 14 years 8 months. PET/CT results have been correlated with conventional imaging (CI), hystologic findings and clinical follow-up.
Results: PET/CT correctly identified pulmonary metastases, according with CI, in 33/56 exams (59%), PET/CT revealed correctly "understaging" in 15 exams (27%) (10 in ES, 5 in OS) and incorrect "understaging" in 8 (14%) exams (4 in OS, 4 in ES). There were no false positive in either groups.
Conclusion: Correct diagnosis of a pulmonary opacity is fundamental for prognosis and choice of treatment in patients with doubtful lung lesions. Our preliminary results suggest the feasibility of a correct characterization by PET/CT in paediatric bone sarcoma patients. In particular PET/CT seems accurate and sensitive for lung nodules higher than 5 mm: an SUV max (and SUV ratio) higher than 1 seems to be significant when size is higher than 5 mm, while no significant SUV max (and SUV ratio) differences were found for smaller lesions. Prospective studies are needed to clarify benefit of PET/CT in management of these patients.

7.O.07

THE INFLUENCE OF SURGICAL AND TUMOUR-RELATED FACTORS ON THE DEVELOPMENT OF LOCAL RECURRENCE IN OSTEOSARCOMA: A RETROSPECTIVE ANALYSIS OF UNSELECTED PATIENTS TREATED ON NEOADJUVANT COOPERATIVE OSTEOSARCOMA STUDY GROUP PROTOCOLS

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The development of local recurrence after multimodal treatment of osteosarcoma is associated with a very poor prognosis. The importance of clear surgical margins has been demonstrated in multiple studies, however up to date there are no studies defining which margin width is safe from an oncological perspective. The purpose of this retrospective analysis was to evaluate whether margin width or other surgical and tumour-related factors influence the development of local recurrence in osteosarcoma patients.
The files of 1867 consecutive patients with high-grade central osteosarcoma of the extremities, the pelvic bones and the shoulder girdle, who had achieved a complete surgical remission during combined-modality therapy on neoadjuvant Cooperative Osteosarcoma Study Group (COSS) protocols between 1986 and 2005, were reviewed. Of those, the data required were available for 1369 patients, who were the subject of this analysis. Eighty of these patients developed a local recurrence during the course of their illness.
The median surgical margin width amounted to 45 mm (range, 0 to 140 mm) in the local recurrence (LR) group and 50 mm (range, 0 to 350 mm) in the non-local recurrence (NLR) group ($p=0.106$). No statistically significant difference between the two groups was found regarding tumour size (mean, 10.38 cm and 9.53 cm respectively, $p=0.169$), T-status ($p=0.225$) and presence of pathological fracture ($p=0.231$). However infiltration of the soft tissue beyond the periosteum was documented in 58.8% of the patients with local recurrence and only in 36.9% of the rest ($p=0.003$). Furthermore, in 50% of the LR group the biopsy had been performed in a centre other than the one performing the definitive tumour resection, compared to 30.2% of the NRL group ($p=0.001$).
In conclusion, the absolute metric width of surgical margins does not define oncological safety. Local recurrence is more likely to develop in patients with soft tissue infiltration beyond the periosteum or those biopsied in a centre other than the one performing the tumour resection.

7.O.08

ZOLEDRONIC ACID AS NEW ADJUVANT THERAPEUTIC AGENT FOR EWING'S SARCOMA

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The development of multi-disciplinary therapy for Ewing's sarcoma (ES) has increased current long-term survival rates to greater than 50%, but only 20% for patients with clinically detectable metastases at diagnosis, or not responding to therapy or with disease relapse. Anti-bone resorption bisphosphonates (BP) may represent promising adjuvant molecules to limit the osteolytic component of bone tumor.
The combination of zoledronic acid (ZOL) and ifosfamide (IFOS) or mafosfamide (MAFOS) was studied in ES models and in 8 human cell lines all expressing the EWS-FLI1 fusion gene. Cell proliferation, viability, apoptosis and cell cycle distribution were analysed. The ES models were developed in immuno-deficient mice by inoculating the human tumor cells either intra-muscular (soft tissue tumor development) or intra-osseous (bone tumor development). Mice were then treated with ZOL (100 g/kg twice or 4 times/week) and/or ifosfamide (IFOS 30 mg/kg, one to 3 sequences of 3 injections).
All the cell lines studied were more or less sensitive to ZOL and MAFOS in terms of cell proliferation. Both drugs induced cell cycle arrest respectively in S and G2M phase and final apoptosis associated to caspase 3 activation. In vivo, ZOL had no effect on soft tumor progression although it dramatically inhibits ES development in bone site. When combined with IFOS, ZOL exerts synergistic effects in the soft tissue model leading to a similar quantitative inhibitory effect when associated with 1 sequence IFOS as compared to 3 sequences of IFOS alone. In the bone model, ZOL prevents tumor recurrence observed with a lonely sequence of IFOS.
Combination of ZOL with conventional chemotherapy showed promising results in both ES models and could allow the clinicians to diminish the doses of chemotherapy. Moreover, as ZOL and MAFOS induce cell death by different pathways, respective resistance may be circumvented.

7.P.01

THE USE OF SILVER-COATED PROXMAL FEMUR OR TIBIA REPLACEMENT AS A PREVENTION OF PERIPROSTHETIC INFECTION. SHORT-TERM RESULTS

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The use of megaprostheses is accompanied with periprosthetic infection in up to 15% of cases. Among metals with antimicrobial activity, silver has raised the interest of investigators because of its good antimicrobial activity. The aim of this study was to determine the infection rate of silver-coated megaprostheses in comparision to uncoated titanium prostheses.
We prospectively identified 40 patients who were treated with a silver-coated proximal femur (n=17) or proximal tibia (n=23) replacement (Mutars®, Implantcast, Germany). Patients with a silver-coated tumor endoprosthesis were compared with 74 (proximal femur replacement n=33, proximal tibia n=41) retrospectively assessed patients with a titanium endoprosthesis regarding the number of infections.
In the titanium group a proximal femur replacement was associated with the highest infection rate (18.2%; time of infection in mean 15 months postoperatively). In the silver-group infection could be reduced to 5.9% (time of infection 12 months postoperatively). In patients with a proximal tibia replacement the infection rate could be reduced from 17.1% (time of infection in mean 28 months postoperatively) to 4.3% (time of infection 4 months postoperatively) in the silver group.
Regarding the final, successful treatment of infection it can be stated that in the silver group the patients could be treated either by intravenous antibiotics only or by a one-stage exchange of the prosthetic body. In the titanium group seven patients (53%) were treated by a two-stage reimplantation of the prosthesis, in 4 patients (31%) an amputation and in one patient rotationplasty was performed.
We conclude that silver-coated megaendoprostheses can reduce the risk of infection on a short-term followup. Importantly, minor revisions in the case of infection in patients with a silver-coated prostheses were more often successful. Further studies with more patients and a longer followup are necessary in order to evaluate the possible benefit of silver exactly.

7.P.02

EFFECTIVE ANTIMIROBIAL ACTIVITY OF SILVER-COATINGS AGAINST SMALL COLONY VARIANTS

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Megaendoprotheses are widely used in the reconstruction of large bone defects in orthopaedic tumour surgery. The major complications (up to 36%) are periprosthetic infections. Persisting periprosthetic infections lead to secondary amputation up to 37% of the cases. One underestimated reason for persisting infections are subpopulations of *S. aureus* called “small colony variants” (SCVs). Aim of this study was to evaluate that silver ions might prevent or cure a periprosthetic infection caused by SCVs.
For testing the antimicrobial activity of silver-coated titanium we used a technique introduced by Bechert et al. Therefore an adhesion and proliferation assay was performed with clinical isolates of *S. aureus* SCV (A22616/3). We tested the adhesion and proliferation properties of *S aureus* SCV on stainless steel (steel), Cobalt-Chrome-Molybdenum-alloy (CoCrMo), Titan-Aluminium-Vanadium-alloy (TiAlVa) and silver-coated Titan-Aluminium-Vanadium-alloy (scTiAlVa).
Adhesion of *S. aureus* SCV is significantly reduced on scTiAlVa vs. steel ($p>0001$). We could also demonstrate that the proliferation rate of scTiAlVa vs. all tested materials is significant ($p>0001$) lower.
We concluded that silver-coating has an effective antimicrobial activity against *S. aureus* SCVs. Thus silver-coated megaendoprostheses are a good prophylaxis against persisting infections caused by *S. aureus* SCVs.

7.P.03

PRELIMINARY EXPERIENCE OF SILVER COATED PROSTHESES IN HIGH RISK PATIENTS

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Aim: To investigate the effectiveness of silver coated titanium prostheses in preventing periprosthetic infection in a group of very high risk patients.
Methods: Periprosthetic infection is one of the main problems in limb salvage surgery, especially for tibial and pelvic prostheses or following revision surgery, particularly if it has been done for a previous infection. We have used silver coated prostheses in 21 cases on a named patient basis and have now assessed the results.
Results: Between July 2006 and June 2008 21 patients had a silver coated prosthesis inserted. 11 patients were having a second stage revision after a previous infection, 6 were having a pelvic prosthesis inserted, 3 were having a primary tibial replacement and one a one stage proximal tibial revision. Three patients developed a postoperative infection, two of the pelvic replacements and one infected revision (a total femur replacement). Of these only one patient required removal of the prosthesis (for overwhelming coliform infection in a pelvic replacement) whilst the other two infections both settled with antibiotics and washout.
Discussion: The anticipated risk of infection in this high risk group would have been around 20%. The actual infection rate was 14% but two of the infections completely resolved with relatively modest treatment. This suggests that the silver coating may not only have a role in preventing infection but also enhancing control of infection should it arise. There were no other side effects and we believe that these preliminary results are encouraging and should lead to a further evaluation of silver for preventing infection around prostheses.

7.P.04

SAINTS COSMAS AND DAMIAN: EUROPE'S FIRST ORTHOPAEDIC ONCOLOGISTS

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Based on paleopathological findings there is evidence that primary malignant bone und probably soft tissue tumours accompanied mankind from the very beginning. Impressive findings of osteosarcomas have been reported from ancient Peru and medieval Hungary. Astonishingly a report exists on a 3rd century AD amputation of a leg affected by "cancer" and, even more amazing, on the successful reconstruction using a homologous limb transplant. This "miracle" has been attributed to Saints Cosmas and Damian. According to the legenda aurea of Jacobo da Varragine the miraculous treatment of took place in 3rd century Rome. The saints amputated the leg of the Deacon Justinian and successfully transplanted the leg of a black African, who had died some hours ago. According to the legend the deacon was able to walk again and glorify his doctors. This legend inspired artists throughout the centuries as can be seen in a famous 16th century oil painting in Stuttgart's Landesmuseum Württemberg. The twin saints Cosmas and Damian have been praised before for the first homoplastic limb transplant. The cause for amputation, however, was reported to be a "gangrenous leg" or a "diseased leg". Looking at the original text of the legenda aurea, a different picture emerges, the cause for surgery being "cancer" of the leg – "…cui cancer unum crus totum cósumpserat". Also astonishing, at their time and in ours, the saints treated patients without taking any payment. It is not surprising that they were the most renowned of all medically inclined saints and were soon regarded as patron saints of medicine. From today's medical view, neither resection margins according to Enneking nor a follow-up period were provided by the legenda aurea. It therefore remains elusive whether a local or systemic recurrence occurred. Nevertheless, Saints Cosmas and Damian may well be regarded as Europe's first orthopaedic oncologists.

7.P.05

STERNAL RESECTIONS FOR PRIMARY OR SECONDARY TUMOURS: SURGICAL MANAGEMENT AND SURVIVAL

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Sternal resection is commonly performed for primary and metastatic chest wall tumours involving the sternum or the ribs near the sternum and, in case of wide resections, it is necessary to restore the stability of the chest wall. We analyze our experience with emphasis on surgical management and survival. From 2001 to 2007, 16 patients underwent surgical resection of the sternum for malignant lesions: 10 (62.5%) primary lesions (chondorsarcoma n=8; osteosarcoma n=2) and 6 (37.5%) secondary lesions (4 local recurrence from breast cancer and 2 metastases). We performed 12 partial resections (resected area from 65 to 20 %), 2 sub-total resections (about 90% of total area) and 1 total resection. Chest wall stability was obtained by prosthetic material, rigid and non rigid, and muscolar flaps. As non rigid material we used a polytetrafluoroethylene patch (Gore-tex Dual Mesh Plus) while replacement after total sternectomy was performed using a new rigid system of mouldable titanium connecting bars and rib clips (Strasbourg Thoracic Osteosyntheses System, Medxpert, GMbH). Prosthetic material was combined in 3 cases with a latissimus dorsi muscolar flap, in 1 case with a vertical rectus abdominis muscolar flap, in 12 with a pectoralis major flap. There was no peri-operative mortality or significant morbidity. All patients were extubated within 24 hours after operation. At a mean follow-up of 44.1 months (range 82-14), 5 years actuarial survival for primary tumours was 85%, while 3 years actuarial survival after resection of secondary tumours was 39% (median 20,5 months). In case of primary lesion wide resection with tumour-free margins is necessary to minimize local recurrence and to contribute to long-term survival; reconstruction with a rigid system composed of mouldable titanium bars and rib clips allows to plan extensive demolition minimizing the risk of chest wall instability. In metastatic disease surgery can provide good palliation, although survival is poor.

7.P.06

EPIPHYSIAL SPARING TECHNIQUES FOR MALIGNANT TUMORS IN CHILDREN USING EPIPHYSIAL DISTRACTION (PAMPLONA TECHNIQUE) AND TRANSEPIPHYSIAL RESECTIONS

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Introduction: Joint sparing is a prerequisite for biologic reconstructions allowing for permanent healing in bone tumors. The physis not crossed by vessels in children can provide a safe margin for tumor resection. In selected patients we have performed joint sparing procedures either by transepiphysial resection or by epiphysial distraction as introduced by Canadell and San Julian.
Patients and methods: 8 children (1 ewing tumor, 8 osteosarcomas [1 multiple localizations]) with open physes 3 distal femurs, 6 proximal tibiae) were treated for metaphysial tumor localizations touching but not crossing to the physis. In 4 localizations epiphysial distraction was used, in the others transepiphysial resection. Reconstructions were performed with vascularized fibula alone in 4 cases, with vascularized fibula transfer and allograft in 1 patient, in the others only intercalary allografts were used.
Results: F/u is 3 to 12 years. No local recurrence occurred. One intercalary allograft failed for infection after irradiation; this was salvaged by a modified rotation plasty. One patient with fibula reconstruction of the femur needed reosteosynthesis due to lack of fusion with a finally excellent result at 3 years f/u, in one the fractured allograft needed be replaced by autologous bone following temporary cement spacer, but the epiphysis could be retained. All patients have excellent joint function. Shortness due to loss of the physis is corrected by contralateral epiphysiodesis and/or lengthening.
Conclusion: Epiphysial sparing tumor resection can be successful oncologically if patients are properly selected and surgery is respecting the tumor margins.

7.P.07

COMPUTER ASSISTED SURGERY (CAS) IN ORTHOPAEDIC ONCOLOGY, TOMTOM OR TOYS FOR THE BOYS?

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In orthopaedic oncology surgical precision is important and intra-operative imaging is often necessary. CAS may enhance precision and provide continuous 3D imaging without radiation. The goal of this work is to report our experience with CAS.
Since 2006 we used CAS (Stryker) in 26 patients with a bone tumour: 11 chondrosarcomas, three osteosarcomas, seven osteochondromas and five miscellaneous. Twelve lesions were located in the femur, six in the pelvis, five in the lower leg and three in the upper extremity. In 18 cases a tumour was excised, in six of these a prosthesis was placed. In eight cases a curettage was done. In 23 cases the navigation was image-based (CT and/or MRI based) and in three cases image-less (no image-preparation necessary preoperatively).
CAS was successfully employed in 23 cases. In three cases the procedure was aborted. In two cases, both in the ulna, we were unable to reconstruct the exact dimensions and in one case (image-less) the tracker was to far away from the work-field. There were no complications related to CAS. Mean precision is 0.5 mm. The time CAS takes is about 15 minutes during the procedure (7-60). In the eight curettages it proved helpful. We did not measure radiation time. In the six resections were tumour-prostheses were placed it was really helpful in rotation and length determination. In three of these, image-less navigation was performed (all distal femur). In osteochondroma resections it is helpful in four of seven cases. All surgical margins were adequate in the resections; after curettage, all MRI controls at three months did not show residual tumour. Oncology follow-up is too short yet; there was one local recurrence after two years in a parosteal osteosarcoma.
We conclude that CAS can be our navigator in orthopaedic oncology; it is successful in providing precision and continuous 3D imaging. The indication area needs further study.

7.P.08

USING MODULAR ENDOPROSTHESIS MUTARS® AT ONCOLOGICAL PATIENTS – OUR EXPERIENCE

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From 1992 on 2008, 615/515 patients underwent primary or revisional endoprosthetic replacement of major joints. In 51 patients (31 men & 20 women) modular system MUTARS (Implantcast, Germany) has been used. The median age was 23.3 years (15 to 52 years). MUTARS modular endoprosthesis has been used in 10 patients with deep infection of endoprosthetic bed as a revisional endoprosthetic replacement: 1 Total endoprosthetic replacement of femur, 5 Total knee joint replacement (2 for distal femoral defect and 3 for proximal tibial defect). In 3(27%) patients, we used newly patented silver ion coated MUTARS either after two stage treatment for infection of endoprosthetic bed or as a prophylaxis of endoprosthetic infection.
In 1 patient (23 yrs), with 12cm limb length shortening, we used extensible MUTARS as a revisional endoprosthetic replacement.
The following complications we observed: Instability of endoprosthesis – 3/51 (5.9%), deep endoprosthetic bed infection – 4/51 (7.8%).
In comparison group, when using custom-made endoprosthesis, the frequency of infectious complications have made 60/574 (10.5 %), and instability of implants was observed in 79/574 (13.8 %) cases.
Transition of using modular systems for primary and revisional endoprosthesis allows to reduce the level of instability from 13.8 % to 5.9 %. The quantity of infectious complications is also not great as in comparison with control group. For revisional endoprosthetic replacement, we think, the given modular system is optimal, for correcting limb length deficiency and restoration of basic function at patients. Use of silver ion coated modular implants is a promising method for treating deep endoprosthetic bed infection.

7.P.09

SURGICAL TREATMENT IN 100 FEMORAL METASTASES

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Introduction: Most of the bone metastases have origin in breast, lung, prostate, thyroid and kidney neoplasms. The commonest locations are the axial skeleton and the proximal region of the long bones, being the femur the most affected one. The main objectives of the surgical treatment are a quick functional recuperation and immediate pain relief.
Objectives: The aim of this work was to define a strategy for the surgical treatment of the bone methastasis located in the femur.
Material: The study includes 94 patients with femoral methastasis (100 metastasis) surgicaly treated in the last 10 years in our department.
Methods: Retrospective descriptive study based on medical records evaluation.
Results: The proximal third of the femur was involved in 80 % of the cases. Pathological fracture was identified in 72 cases and impending fracture in 28. Half of the primitive neoplasms was originated in the breast. It was identified as solitary metastatic lesion only in 33 % of the situations. The mean patient survival time was 9,2 months. They were treated with a cemented calcar-replacing prosthesis in 40 patients, 10 patients submited to conventional arthroplasty and 36 with intramedullary fixation (usually a cephalomedullary nail). The remainder 14 were treated with other surgical techniques.
Discussion: The surgery is indicated in case of painful lytic injury or unresponsive to radiotherapy, pathological or impending fracture. The surgical technique depends on the location and size of the lesion and if it is a solitary or multiple bone lesion, choosing between arthroplasties, of preference with long femoral stem, and intramedullary fixation. As we have performed a retrospective study, a functional rigorous evaluation was not possible.
Conclusion: The treatment of metastatic femoral disease is not performed with the intention of cure but to improve significantly the patient's life quality. The proximal third of the femur is the most reached place. Breast cancer was responsible for around 50 % of the cases. In 50% of the patients the surgical option was an arthroplasty and techniques of femoral nailing were performed in 36%. The cemented replacement prosthesis is used in proximal large injuries with periarticular involvement: The intramedullary fixation is reserved for situations in which the femoral head and neck are not involved. The length of patient survival must exceed the predictable surgical recovery period.

7.P.10

EVALUATION OF STABILITY OF ROTATING HINGE KNEE PROSTHESES: A BIOMECHANICAL ANALYSIS

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Introduction: Rotating hinge knee prostheses are designed to provide a stable knee reconstruction when the intrinsic soft-tissue stability of the knee had been lost as a result of tumor resection, multiple knee replacements, trauma or surgical reconstruction. Instability is the main risk factor for implant´s dislocation. We performed a biomechanical analysis to establish the association between design of the central rotational stem (length and taper) and the implant´s stability, using a self constructed biomechanical apparatus on a test bench in the laboratory.
Materials and Methods: The lengths and tapers of the central rotational stem of three different rotating hinge knee implants (LPS/M.B.T. (DePuy)-cylindrical, length: 46mm, taper: 0°; S-ROM Noiles (DePuy) -conical, length: 46mm, taper: 5°; GMRS (Howmedica) -cylindrical, length: 47mm, taper: 0°) were measured using a self-constructed biomechanical testing device. The degree of tilting of the central rotational stem within the vertical post-in channel by extending the distraction was measured as well the maximum amount of distraction before the stem's dislocation.
Results: The GMRS implant design was superior to the LPS/M.B.T. and the S-ROM Noiles implant design concerning stability and maximum amount of distraction before dislocation (38 vs. 27 vs. 26 mm). The GMRS system had a steep rising distraction-angular displacement curve until the dislocation at 38mm occurred while the laxity curve of S-ROM Noiles showed a poor increasement. Besides early high laxity it required only 26mm of distraction to dislocate.
Conclusions: Our conclusion is that rotating hinge prostheses with a short and markedly tapered central rotational stem have the highest instability / angular laxity at any given amount of distraction. Such knee prostheses should be used with caution in patients after excessive soft tissue resection. A long and cylindrical central rotational stem seems to prevent early instability and implant's dislocation.

7.P.11

CT GUIDED RADIO FREQUENCY ABLATION OF PEDIATRIC OSTEOID OSTEOMA UTILIZING A WATER-COOLED TIP

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Radiofrequency (RF) ablation carries success rate of 70-90% in the treatment of Osteoid Osteoma (OO). Failures are related to incomplete ablation which might be caused by the probe's small heating radius (0.5-0.8 cm). Water cooled tips were developed in order to prevent charring of the tip and adjacent tissues and to allow for a larger, up to 3cm ablation diameter. To our knowledge safety and efficiency of this probe in the treatment of pediatric OO were never reported. Our goal was to examine if this technique, when added to conventional RF ablation, improves the clinical results and whether it carries any additional risks in the pediatric population.
Twenty two OO patients, 15 males and 7 females, 3 years and 6 months to 18 years old, were treated using the Cool-tip™ Tyco probe in a cooled mode followed immediately by conventional RF cycle under general anesthesia, in the CT suite. Fifteen of the lesions were in the femur, 2 in the tibia and the remainder lesions were located in the humerus, talus, calcaneus, 2nd metatarsus and sacrum. The OO was intraarticular in 5 patients: femur (3), calcaneus and Talus. Follow-up period averaged 38.5 months (range 16-66 months). All patients but one had their symptoms resolved immediately following a single treatment (95.5% success rate). One patient had partial relief and underwent second successful ablation. There were one recurrence after 18 months and one superficial infection. No fractures, neuro-vascular complications or growth disturbances were eWe conclude that the addition of a Cool-tip cycle to conventional RF ablation in children is safe, efficient and reduces the risk of recurrence without adverse effects specific to this age group. We attribute this success to the larger diameter of heat distribution occurring due to cooling of the tip and the prevention of probe and tissue charring.

7.P.12

CLASSIFICATION OF SPINOPELVIC RESECTIONS: ONCOLOGIC AND RECONSTRUCTIVE IMPLICATIONS

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Curative treatment of malignancies in the sacrum and lower lumbar spine frequently requires en bloc spinopelvic resection. There is no standard classification of these procedures. We present outcomes and a classification scheme with oncologic and reconstructive guidelines for spinopelvic tumors based on an analysis of 30 cases of en bloc resection and reconstruction performed with curative intent.
Mean follow-up of surviving patients was 38 months. Tumors included osteosarcoma (n=9), chondrosarcoma (n=6), chordoma (n=5), other sarcomas (n=5), neurogenic tumors (n=4), and local extension of carcinoma (n=1). Resections could be divided into 4 types. Type 1 resections (n=12) included a total sacrectomy with lower lumbar spine and bilateral medial iliac resections. Type 2 resections (n=6) included hemisacrectomy, partial lumbar spine excision, and medial iliac resection. Type 3 resections (n=9) encompassed external hemipelvectomy with hemisacrectomy and partial lumbar spine excision. Type 4 resections (n=3) encompassed external hemipelvectomy, total sacrectomy, and lumbar spine excision. For each resection type, we have developed staged surgical approaches to allow resection with wide margins and reconstruction of spinopelvic continuity. Tumor free margins were achieved in all cases. Perioperative mortality was 3/30. Seven additional patients have died of disease, two died of other causes, two are alive with disease, and 16 have no evidence of disease. 13/18 surviving patients are independent in their activities of daily living.
In our practice en bloc excision and reconstruction of spinopelvic neoplasms may be classified into four types. For each type, we have devised surgical treatment guidelines to allow for wide resection and reconstruction of spinopelvic continuity. Long term survival and independent function can be achieved in this challenging patient population. This represents the first standardised classification of oncologic spinopelvic resections and reconstructions.

7.P.13

THE INTERPELVIC-ABDOMINAL AMPUTATION IN COMBINED TREATMENT OF MALIGNANT TUMORS OF THE PELVIC WAIST

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The results of treatment of 45 patients with malignant bone tumors and soft tissues of thigh proximal part and pelvis have been analyzed in the work. From 45 male patients -37 (82%), women -8 (18%). Patients' age varied from 17-to 53 years old, in average was-33 year old. In 22 patients the tumor localized in thigh proximal part, in 17 – in the bone and soft pelvic tissues, in 2- in the buttock part and in 4- noticed metastasis lesion inguinal-iliac lymph nodes. In 5 observations histological type composed from malignant gigantic cellular tumor, in 8 osteogen sarcomas, in 11-hondrosarcomas, in 5-Ewing's sarcomas, in 4 - fibrosarcoma of soft tissues, in 4-rabdomiosarcomas, in 1- angiosarcoma of soft tissues, in 1-leiomyosarcomas, in 1-synovial sarcomas, in 1- polymorph cellular sarcomas of soft tissues and in 4- marked metastasis lesion (mainly flat cellular skin cancer) lymph nodes of inguinal-iliac part. The complex diagnostic measures including clinic, X-ray and ultrasound diagnostics, angiography, computed magnetic – resonance tomography and morphologic investigations were carried out with all patients.
A size of tumor process is 250-450cm^3. In all cases carried out lymph dissection with removing of cellular tissue of pelvis till bifurcation of abdominal aorta, in 5 additionally are made sacrum resection. Duration of operational interference was from 150 to 189 minutes, and blood lost - from 1200 to 1800 ml. There were no mortality outcomes during the operation. The patients have been observed from 1 year till 12 years. During observation period from 45 patients in 4 (8%) have been determined local recurrence, in 12 (26%) - separated metastasis and in 2 (4%) –simultaneously determined recurring and separated metastasis. Findings of 3 and 5 years survival are 44,6% and 33,5%.
So, interpelvic-abdominal amputation prolongs patients' surveillance, which before is considered hopeless and mainly undergone palliative chemotherapy and symptomatic treatment.

7.P.14

IMAGING-GUIDED CORE NEEDLE BIOPSY: A STUDY OF 412 PATIENTS

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Core needle
From the other 335, 116 were benign tumours or tumour-like conditions, 86 primary malignant, 53 lesions oh Hematopoietic, lymphoid and biopsy is simple, practical and easily permits diagnosis of bone and soft tissue tumours and tumour-like conditions even when immunohistochemical studies are needed.
We present the results of 412 core needle biopsies guided with fluoroscopy, CT and echo scan with assessment of accuracy and costs
From January/96 to December/08, 56 soft tissue and 356 bone tumours and tumour-like lesions were submitted to this technique in the Oncology Unit of Hospital Santo António. All biopsies were performed by the same team (one radiologist, one orthopaedic surgeon) and the histological exam by the same pathologist.
There were 77 cases in which diagnosis was inconclusive (sample not representative, crushing, necrosis, hemorrhagic features or image/histological dissociation); 36 of these were soft tissue and 41 bone lesions. histiocytic elements, 65 metastases, 8 recurrent malignancies, 5 osteomyelitis and 2 metabolic diseases.
Diagnosis was confirmed in 278 cases with the definitive surgery and only one was wrong. The other 57 cases were later controlled by imaging exams and there were no reasons to suspect a wrong diagnosis.

No complications occurred.

Costs were estimated to be less than one fifth of an open biopsy.

The high accuracy (only one case was misdiagnosis), the safety, the costs and the fact that in only 18,7% the diagnosis was not established make us consider this method effective and to be encouraged. Better selection of lesions and more attention to directions of the cores may low the number of inconclusive diagnosis.

7.P.15

VASCULARISED FIBULA WITH SKIN-FLAP IN INFECTED FOOT AND ANKLE RECONSTRUCTIONS AFTER ONCOLOGICAL RESECTION

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In oncological resections there is a higher risk of infection around the foot and ankle. An infection here can be difficult to treat and easily lead to an amputation due to the limited amount of soft tissue coverage of the region. In three patients an infection developed after resection of a bone tumour in the foot and ankle.
In the first case, female 34 years, an epitheloid hemangioepithelioma was excised from the anterior part of the calcaneus, cuboid and lateral os cuneiform. An iliac crest graft was initially used to fill the defect, but got infected. The antibiotic loaded bone cement spacer cured the infection and filled the dead space but was painful. A free vascularised fibula with skin-flap was used successfully to fill the defect and take away the pain. At three-year follow-up there is no pain and full weight bearing, with a nice hypertrophy of the graft. In the second case, a 14-year old girl, there was an Aneurismal Bone Cyst (ABC) of the distal tibia with a deep infection after ethibloc injection. The vacuum assisted closure cleaned the wound but a defect resulted. It was successfully filled with an ipsilateral free vascularised fibula with skin-flap. Follow-up shows full function and nice hypertrophy at 24 months. In the third case, male 65 years, a chondrosarcoma grade one (after biopsy) in the cuboid was curetted out. It proved grade two in the definitive histology and furthermore it got infected. The cuboid was excised and a cement spacer was placed. The soft tissues were insufficient to close it properly. A free vascularised fibula with skin-flap was used. The vascularity of the graft was insufficient and the skin-flap did not survive. A vacuum assisted closure was done. He can bear weight and has no pain. The fibula graft is shows some hypertrophy and a fistula persists for 18 months now.
We conclude that vascularised free fibula with skin-flap can successfully prevent amputation in case of infection in oncological resection of foot and ankle. The fibula reconstructs the bone defect and the skin-flap the soft tissue defect.

7.P.16

THE SELECTION OF SURGICAL INTERVENTION VOLUME IN LOCAL SPREAD TUMORS OF SHOULDER GIRDLE

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We observed the 55 patients with local spread tumours of bones and soft tissues of shoulder girdle. There were 43 (78,2%) men, 12 (21,8%) women; the average age was 38,8. In 23 patients the tumour became localized into proximal part of humerus, 2 were in lateral end of clavicle, 4 were in shoulder blade, 18 were in soft tissues of upper two thirds of shoulder, 4 were in soft tissues of axiila, 3 were in soft tissues of shoulder blade and 1 was metastases of sarcoma of forearm soft tissues in armpit lymph nodes. In 8 cases the bone tumours were presented with osteosarcoma, 12 - hondrosarcoma, 5 - malignant giant celled tumour, 1 - Ewing's sarcoma, 1 - reticulosarcoma, 2 - fibrosarcoma of bone. Among tumours of soft tissues, the fibrosarcoma and synovial sarcoma prevailed over 10 and 8.
Regard for local spread of tumour and degree of anatomical structures drawing in process, 47 patients performed interscapulothoracic amputation and 8 were interscapulothoracic resection (Tikhoff-Linberg operation). In pre- and post operative period the chemical and/or radiotherapy were performed in 43 patients. Selection the scheme and regimen of treatment depended on histological type of tumour.
The dates of observation were from 6 month to 14 years. The acute disorder of cerebral blood circulation was developed in one patient after interscapulothoracic amputation in early postoperative period. The local recurrence of tumour was revealed in 4 patients (8,4%) after interscapulothoracic amputation and in 3 patients (37,5%) after interscapulothoracic resection, in 14 (29,7%) and 4 (50%) were metastases conditionally. All patients had local recurrence in soft tissues. In 2 patients with local recurrence the amputation of extremities were performed.
There fore, the interscapulothoracic resection is used in local spread tumours of proximal part of humerus, shoulder blade, acromical part of clavicle and soft tissues of shoulder girdle, with some anatomical structures involved in process, but without affection of vascular-nerve fascicules. Involving in tumor process vascular and nerve plexus are statement for performing interscapulothoracic amputation.

7.P.17

A NEW METHOD OF RECONSTRUCTION FOLLOWING FULL THICKNESS CHEST WALL RESECTIONS

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Chondrosarcoma is an uncommon primary malignancy of cartilage. This tumour tends to be resistant to both chemotherapy and radiotherapy making surgical resection the primary treatment. These tumours can present on the chest wall, requiring multidisciplinary team input at the time of surgery, involving orthopaedic, cardiothoracic and plastic surgeons. Complete excision, ensuring adequate resection margins, requires removal of ribs and pleura resulting in a full thickness chest wall defect. Complex reconstruction techniques are necessary to prevent post-operative morbidity of chest wall indrawing and reduced pulmonary function. Reconstruction can be considered in two parts, the reconstruction of the rigid support and the necessary soft tissue cover. In the past a number of options have been available to provide the rigid support, marlex sandwich, prolene mesh and autologous bone grafting. Each of these techniques has potential disadvantages.
We describe two patients who underwent resection of chest wall chondrosarcomas. These patients had reconstruction of the rigid chest wall support using STRATOS (STRASBOURG Thoracic Osteosyntheses System). This system utilises clamps around the cut ends of the ribs to provide the necessary rigid support, eliminating some of the disadvantages of the older techniques. Both patients made an uncomplicated post-operative recovery.
The STRATOS implant was easily used and versatile, providing an immediately secure and rigid fixation in chest wall reconstruction.

7.P.18

INTRAMEDULLARY DIAPHYSEAL SEGMENTAL FIXATION SYSTEM FOR LIMB SALVAGE AFTER TUMOUR RESECTION

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Six patients underwent wide segmental resection and limb salvage surgery for primary or metastatic bone tumors involving the diaphysis of the femur, the tibia and the humerus using a modular intramedullary diaphyseal segmental defect fixation system. There were 4 men and 2 women with a mean age of 62 years (range, 40 to 77 years).
Histological diagnosis included adamantinoma, dedifferentiated synovial sarcoma attached to the tibia, multiple myeloma, and metastatic renal cell carcinoma, myeloid carcinoma of the thyroid gland and metastatic adenocarcinoma of the stomach.
The mean follow-up was 16 months (range, 11 to 24 months). At the latest examination, 5 patients were free of local or distant disease; one patient had deceased with distant disease, without evidence of local recurrence. Revision surgery was necessary in one patient because of mechanical loosening of the proximal fixation of the prosthesis. The mean increase of the Enneking rating from the pre to the postoperative status was 87.82% .
The intramedullary diaphyseal segmental defect fixation system used herein is associated with a satisfactory functional and oncological outcome after wide resection of diaphyseal bone tumors.

7.P.19

RADIOTHERAPY IN OSTEOSARCOMA

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The experience of radiotherapy (RT) in the local treatment of osteosarcoma (OS) is limited. Data of 100 patients with RT for OS from the international COSS-Registry (1980-2007) were analysed. Survival and local control rates at five years were calculated. Univariate and multivariate analyses were performed.
The COSS-registry includes 3500 patients with histologically proven OS. A total of 175 patients were irradiated over the period of 1980 to 2007, 100 patients were eligible. Median age was 18 (3-66) years. Indication for RT was a primary tumor in 66, a local recurrence in 11 and metastases in 23 patients. 94 Patients got external photontherapy, 2 pats. protontherapy, 2 pats. neutrontherapy, and 2 pats. intraoperative RT. Seventeen patients received a samarium-153-EDTMP therapy. Median dose for external RT was 55.8 Gy All patients were treated with chemotherapy in accordance to different COSS-protocols.
Median follow-up is 1.5 (0.2-23) years. Overall survival rates at 5 years for the whole group, for treatment of primary tumours, local recurrence, and metastases are 36 %, 55%, 15%, and 0% respectively. Local control rate for combined surgery and RT is significantly better than for RT alone (48% vs. 22%, p=0.002). Local control for treatment of primary tumours, local recurrence, and metastases are 40%, 17%, and 0% respectively. Prognostic factors for survival are indication for RT, RT plus surgery vs. RT alone and localisation. Prognostic factors for local control are indication for RT, and RT plus surgery vs. RT alone.
Radiotherapy is an important option for local treatment of unresectable OS, after intralesional resection, or symptomatic metastases. Survival prognosis of these patients is poor. Combination of surgery, radiotherapy, and chemotherapy can be curative. Prognostic factors were identified.

7.P.20

THE ROLE OF PREOPERATIVE RADIOTHERAPY +/- NEOADJUVANT CHEMOTHERAPY IN NONMETASTATIC SOFT TISSUE SARCOMAS OF THE EXTREMITIES FOR LIMB-SPARING SURGERY: A SINGLE INSTITUTION RESULTS

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Our purpose was to assess the role of preoperative radiotherapy +/- neoadjuvant chemotherapy in nonmetastatic soft tissue sarcoma of extremities for limb-sparing surgery and identify the role of neoadjuvant therapies on local control and survival rate.
Forty-seven patients with soft tissue sarcoma of extremities who were treated at Cerrahpasa Medical Faculty within a limb salvage protocol, including preoperative radiotherapy +/- chemotherapy were retrospectively analized. Median age was 45 years (17-72 years).The tumor size was between 5-33 cm. Seventeen patients were in stage I, 11 in stage II, 19 in stage III. The most common histology was synovial sarcoma. Nine patients were treated for locally recurrent tumour. The tumour and surrounding tissues with probable microscopic tumour involvement observed clinically and radiologically, were irradiated. Thirty-two patients, with a high grade tumour and/or tumours larger than 8 cm, also received neoadjuvant chemotherapy. Neoadjuvant chemotherapy regimen was consisted of doxorubicine and ifosphamide with mesna. Preoperative radiotherapy was applied, usually between the second and third cycles of chemotherapy. Definitive surgery was administered 2-6 weeks after radiotherapy or after the third cycle of chemotherapy. Chemotherapy was completed to 6 courses after the surgery. Postoperative external beam radiotherapy boost of 16 Gy was given who had close or positive surgical margins. Median follow-up time was 67 months (12–217 months). All of the patients had limb-sparing surgery. Patients had; 30 marginal excision, 13 wide local excision, 4 radical resection. Nine patients locally recurred. Limb-sparing surgery was performed for 8 patients. 25 patients had distant metastases. Metastasectomy were applied for 10 patients with lung metastasis. The 5-year local control, disease free survival and overall survival rates were 82.3%, 50.1% and 67.2%, respectively.
Preoperative radiotherapy +/- chemotherapy seems to increase the chance of extremity-sparing surgery with good local control and the survival rates which were comparable with the literature.

7.P.21

OSTEOID OSTEOMA: 20 PATIENTS TREATED WITH RADIOFREQUENCY

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Osteoid osteomas are benign, painful osteogenic tumours of small size (≤ 1,5 cm). Surgical resection of the nidus has been the elected method of treatment for decades but some complications and difficulties (poor localization, extensive tissue damage, fractures, delayed recovery) encouraged the development of less invasive techniques such asLack of histological proof is the major concern regarding radiofrequency ablation as we make the diagnosis by the clinical findings and the image features.
We present the results of 20 patients with osteoid osteoma treated with radiofrequency from January 2004 to December 2008 (mean follow up 23 months). All patients were under general anaesthesia and de access route was chosen in the CT-suite. 11 cases were located in the proximal femur (head, neck and subtrocanteric region), 2 in the distal femur, 2 in de distal humerus, 2 in the tibia, 2 in the acetabulum, and 1 in de vertebal body of D8.
In all cases we used a Cool-tip ™RF electrode (water-cooled tip) reaching a heating temperature of 42ºC to 48ºC during 12 minutes. In 7 patients a cannulated drill bit was used to penetrate the thick cortical or to reach the nidus through the opposite side in order to avoid a neurovascular bundle.
Hospital discharge was allowed after 6 to 8 hours after the procedure.
No complications occurred.
All patients, except one, experienced complete relief of the pain although the 6- month follow-up CT's do not show sclerosis of the nidus. None of them recurred till data. The patient who did not recover had not had a clear diagnosis.
We conclude that radiofrequency ablation is effective, safe, favouring rapid recovery and, of course, reduces economical and social costs.

7.P.22

RETROSPECTIVE ANALYSIS OF SIMULTANEOUS RADIOCHEMOTHERAPY WITH SINGLE-AGENT IFOSFAMIDE IN PATIENTS WITH MACROSCOPIC SOFT TISSUE SARCOMA

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Standard therapy for soft-tissue sarcomas remains complete resection, irresectable tumours or tumours after resection with gross residual disease are a special challenge. For primary radiotherapy with median 60 Gy local control rates of 30-45% have been reported. We analysed retrospectively 11 cases of radiochemotherapy with single-agent Ifosfamide in patients with macroscopic soft-tissue sarcomas.
The patients were treated in irresectable high risk situations: T2-tumours (100%), G3 (73%), localisation at the trunk (82%). Radiation therapy was performed with median 60 Gy (50 to 72.6 Gy) in 1.8-2.0 Gy single fraction dose, once daily, five times a week. During the first and fifth week the concommittant chemotherapy with 1.0/1.5 gr/m2/d Ifosfamide on five days was added. Two patients received trimodal therapy with additional hyperthermia. The therapy was completed in 73% of the patients. Average local control time was 91 months, median disease-free-survival/overall-survival was 8/26 months. Five-year rates for local control/disease free survival/overall survival were 70%/34%/34%. Long-term tumor control could be achieved in three patients. The median disease free survival is dependant on the histological tumor grading (21 vs 8 months for G2 vs G3 tumors, no statistical significance due to small patient numbers). The limited prognosis is mainly caused by systemic treatment failure.
Additional concommittant radiotherapy should be considered for irresectable soft tissue sarcomas or tumors after resection with gross residual disease, if the applicable radiation dose is limited due to close vicinity of organs at risk.

7.P.23

RADIO FREQUENCY ABLATION (RFA) IN ORTHOPAEDIC ONCOLOGY; INDICATIONS AND COMPLICATIONS

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Radio Frequency Ablation (RFA) is a precise CT-guided technique to generate a small pre-defined field of dissecated tissue. Its' present use in orthopaedic oncology is to treat osteoid osteoma. We have also treated other lesions with RFA and want to report our present indications and complications.
From 2005 to 2008 we performed 30 procedures: 23 osteoid osteomas, five low-grade chondrosarcomas, one chondroblastoma and one thyroid metastasis. Localisations were femur in 14 cases, tibia in 10, calcaneus in two, fibula in two, sacrum in one and scapula in one. All patients were treated with CT- guided RFA (Boston Scientific).
Follow-up for osteoid osteoma was done without additional imaging, all patients but one were pain free within 2 weeks; this one patient proved to have a chronic osteomyelitis although we thought we saw a nidus on CT. In one patient a burn wound complicated treatment because of unnoticed damage of the isolation layer of the probe. A free skin graft was necessary. We performed MRI controls and curettages for the chondrosarcomas in three patients, in one patient a fracture developed in the calcar femoris region after three months and a hip replacement was done. The patient with chondroblastoma is followed by MRI and there is no activity on contrast MRI two years after the procedure. In one lady a RFA was done for thyroid metastasis in the calcar femoris region. She fractured her collum femoris and got a hip replacement. In all tissue retrieved after RFA (curettage and hip replacement), there was complete necrosis of the tumour (chondrosarcoma grade one and thyroid metastasis).
RFA is an effective procedure for osteoid osteoma. Fracture and skin burns can occur. It is promising in low-grade chondrosarcoma and chondroblastoma. A study has been initiated recently to evaluate effectiveness of RFA in low-grade chondrosarcoma < 4 cm.

7.P.24

EXTRACORPOREAL IRRADIATION AND RE-IMPLANTATION OF TUMOR BEARING BONES

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Extracorporeal Irradiation and Re-implantation (EIR) of tumor bearing bone segments is an alternative reconstruction method for major osseous resections. In contrast with endoprosthetic reconstruction, EIR is a biologic solution and after a prolonged healing and remodeling period it is expected to create a structural and metabolic almost normal bone. After oncologic resection the bone segment is cleaned from adhered soft tissues and send to irradiation which kills malignant and normal cells. Re-implantation consists of fixation, mostly by plates, vascularised fibular graft insertion in the medullary canal, iliac bone graft in critical sites and ligamentous sutures.

Since 2001 fifteen patients were submitted to EIR in our institution. Resections affected seven distal femurs, four proximal tibias, one acetabulum, one iliac bone and the proximal forehand bones once which bear 11 osteosarcomas, 2 Ewing's sarcomas, 1 chondrosarcoma and 1 rhabdomyosarcoma. There were six males and nine females with age ranging from five to 55 years. Ten patients were submitted to osteoarticular reconstructions, three to intercalary and two to partial pelvis reconstructions.

Local recurrence leading to amputation occurred in one patient and resection of an infected innominate bone occurred once. Three patients died two to nine months after surgery because of their disease. Five patients had metaphyseal fractures after one to 14 months after surgery. Four patients had no fracture; three of them had intercalary resections. The patient with osteoarticular resection and no fracture had his metaphyseal region injected with cement which prevented fracture and after 23 months have not developed osteoarthritis.

All the cases in which a vascularised fibular graft was implanted progressive fusion of the living and dead bones were observed.

As a conclusion EIR is a good alternative for intercalary resections. For osteoarticular resections improvement of the method are necessary to prevent fracture and ligamentous laxity.

7.P.25

PATTERN OF ARTICULAR INVASION IN BONE SARCOMAS AROUND THE KNEE

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Articular invasion by malignant bone tumours around the knee is one of the most important criterions to determine prior surgery. MR imaging is the most accurate exam in staging bone sarcomas. Although, past studies showed that when MRI shows evidence of intra articular involvement by tumour, the incidence of false positive diagnosis and subsequent excessively radical surgery is as high as 50%. The aim of this study is to determine growth pattern of bone sarcomas into the joint in order to assess which are the limits of the joint compartment.
We reviewed retrospectively 18 cases of primary intra medullary sarcomas with epiphyseal extension located around the knee. The tumour was located in the distal femur in 11 cases and in the proximal tibia in 7 cases. In tumours located in the distal femur, two distinct modes of extension towards synovium and joint space were identified. The most common pattern was tumour growth along the anterior and intra articular part of the distal femur. This pattern was observed in 10 cases. The tumour displaced anteriorly soft tissues and remained extra synovial in 6 cases. Only in 4 cases, tumour contaminated the joint space. The extension was in all cases marginally close to the cartilage of the trochlea in the transitional zone between cartilage and synovial membrane.
The second pattern was extension through the inter condylar notch which was observed in three cases. Growth was around the osseous-tendinous junction of the cruciate ligaments and never within the ligament.
In tumors in the proximal tibia, although tumour was close to the osteochondral junction, cartilage was not breached anyway. Tumour got around the cartilage. Extension of the tumour to the articular joint was marginally under the posterior capsule insertions making contact with the edge of the articular cartilage. This pattern was observed in two cases. We didn't observe an erosion of cartilage layer, in the limits of the sections done.
Our study, demonstrated that cartilage and synovial membrane, since they are not breached, represent reliable margins for intra articular resections. We identified in the current study, one mode of tumour extension towards synovium and joint space. In all cases, extension was in junctional zones between cartilage and synovial membrane or cartilage and articular capsule. The articular cartilage was the most resistant barrier, having no vascular perforations and probably an intrinsic resistance to tumour.

7.P.26

SYSTEMIC INFECTION BY MYCOBACTERIUM XENOPI MIMICKING MULTIPLE PULMONARY METASTASES OF AN OSTEOBLASTIC OSTEOSARCOMA

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We report on a patient with an unusual pulmonary infection after resection of a high-grade osteosarcoma.
In March 2007 a 30-year old female with pain and swelling of the left proximal humerus was submitted to the orthopaedic department. Rx and CT revealed a tumour with destruction and invasion of the surrounding soft tissue.
Incision biopsy led to the diagnosis of osteoblastic osteosarcoma. She was enrolled into the EURAMOS protocol and received neoadjuvant chemotherapy. In July 2007 an extra-articular resection of the proximal humerus with modular endoprosthetic replacement was performed. The sarcoma had responded well to chemotherapy (regression grade 3 according to Salzer-Kuntschik). Surprisingly, the resection specimen demonstrated a “skip lesion” of vital sarcoma in the resection line not been detected by preoperative PET or MRT. After consultation of the German study group she was stratified into the standard risk group.
12 months later a control CT revealed multiple foci in both lungs, which were highly suspicious for pulmonary metastases. All clinical parameters were normal. A lung biopsy was performed by thoracotomy and a granulomatous infection was diagnosed, which was suspicious for tuberculosis. Extended microbiological investigations by culture and PCR analysis revealed an infection by Mycobacterium Xenopi, which is a rare form of an atypical mycobacteriosis. Since then she is treated accordingly, however the infection has progressed and involvement of the liver has been diagnosed by cutting needle biopsy.

7.P.27

POSSIBILITIES OF ULTRASOUND DOPPLEROGRAPHY IN THE TREATMENT AND MONITORING OF PATIENTS WITH MALIGNANT TUMORS OF BONES AND SOFT TISSUES

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The aim of the research was to improve the results of complex ray diagnostics and monitoring in the treatment stages of patients with malignant neoplasms of soft tissues and bones using ultrasound dopplerography (US-dopplerography).
US-dopplerography data in 38 patients with tumors of soft tissues and bone tumors with infiltrated soft tissues are studied in the course of treatment. The following criteria were investigated by dopplerography: arterio-venous blood-flow, venous blood-flow, maximal velocity (V_{max}) of blood, minimal velocity (V_{min}) of blood, index of resistance (IR), pulse index (PI).
In 7of 38 patients US-dopplerography was performed repeatedly in dynamics. In 2 patients with fibrosarcoma character of neoplasm tissue blood-flow changed: in 1 patient after combined chemo- and ray-therapy neoplasm tissue blood-flow was not registered practically, in the 2nd patient indices of blood-flow decreased after chemotherapy. In 8 patients presented with fibrosarcoma blood-flow was not detected in the structure of neoplasm, and in 3 patients with the same diagnosis moderate peripheral blood-flow in the neoplasm was revealed. In one patient with osteosarcoma parameters of blood-flow in soft tissues infiltration were not changed even after 4 courses of chemotherapy. In the second patient parameters of blood-flow increased after 1st course of chemotherapy treatment, and after 3rd course blood-flow in the damaged area practically could not be detected. In 2 patients, presented with neuroblastoma and Khodjkin's lymphoma, parameters of blood-flow decreased until complete disappearance after 2 courses of chemotherapy. In one patient with rhabdomyosarcoma blood-flow indices did not actually change in the process of treatment.
Parameters of US-dopplerography in dynamic control can serve as an indicator in the treatment efficacy assessment in patients with soft tissue and bone tumors.

7.P.28

FACTORS DETERMINING SURVIVAL AFTER RESECTION OF PULMONARY METASTASIS OF HIGH GRADE OSTEOSARCOMA

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Resection of pulmonary metastases has previously been reported to improve outcome in high grade osteosarcoma (OS) patients with pulmonary metastases. In this study factors influencing survival in OS patients with pulmonary metastases were determined.
One hundred ninety seven patients with OS treated at our institution between 1990 and 2008 under the age of 40 were included. Excluded were patients with insufficient follow-up data (n=12) and irresectable primary tumour (n=11). Of the 174 remaining patients, 26 patients had pulmonary metastases at diagnosis and 62 developed pulmonary metastases during follow-up. Twenty-two of 88 patients (25%) also had extra-pulmonary metastases. Almost all patients with primary non-metastatic OS who experienced a relapse within 310 days (first tertile) died of disease, whereas patients with a relapse free interval of more than 310 days (second and third tertiles) have a significantly better overall survival at about 20% (p=0.02). In total, 56 (63.6%) of 88 patients with pulmonary metastases were treated by metastasectomy. The main reason not to perform metastasectomy was irresectability by number and site. Patients with irresectable pulmonary metastases had higher numbers of pulmonary nodules (mean of six *vs.* three nodules) and more frequent bilateral involvement than patients eligible for surgery (p-values respectively 0.002 and 0.06). Independent risk factors determining survival after metastasectomy in multivariate analysis were male sex (p=0.05), higher numbers of pulmonary nodules (p=0.03) and necrotic metastases (p=0.04). Patients undergoing repeated metastasectomies had a similar chance of survival as patients who underwent metastasectomy once.
This well-defined cohort of patients with extensive follow-up data enabled us to identify important risk factors determining survival in OS patients with pulmonary metastases. Risk factors determining poor survival after pulmonary metastasectomy were male sex, higher numbers of pulmonary nodules and resection of vital metastases. Furthermore, we demonstrate that even after repeated metastasectomies, curation can be achieved.

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7.P.29

A PILOT PHARMACOGENOMIC STUDY OF THE INFLUENCE OF CYTOTOXIC TARGET AND METABOLISING GENE POLYMORPHISMS ON TOXICITY AND RESPONSE IN OSTEOSARCOMA

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Osteosarcoma is the most common malignant bone tumour in children and young people. Approximately 40% patients respond poorly to highly toxic pre-operative MAP (methotrexate adriamycin, cisplatin) chemotherapy with consequent inferior survival. The role of genetic polymorphisms in drug response and toxicity is reported in acute leukaemia and some solid tumours. Recent evidence in osteosarcoma suggests increased chemotherapy toxicity is associated with improved survival. The aim of this pilot study is to investigate the influence of drug target and metabolising gene polymorphisms on tumour response and chemotherapy toxicity in osteosarcoma.

Patients who have completed MAP chemotherapy are eligible. Chemotherapy toxicity (CTCAE grade) is collected from patient records. Tumour response is graded as good (>90% necrosis) or poor (< 90% necrosis) in resection specimen. Peripheral blood DNA is typed for genome-wide single nucleotide polymorphisms (SNP) using the Illumina 610 Quad array and analysed using Bead Studio software. Standard PCR techniques are used to genotype the Thymidylate synthase (TS) gene (folate pathway) for the presence of 2 or 3 copies of a 28 base pair repeat (2R/3R) and a G/C SNP in the 3R allele.

52 patients have entered to date: 33 good responders, 12 poor and 7 unevaluable for response. Median age 18 years (range 10-51), males:females 1.3:1. Median follow up is 39 months (range 2-76) with 11 patients relapsing. 23 patients have TS genotype 2R/2R, nineteen 2R/3R, six 3R/3R, three 2R/4R and one 2R/7R. Neither TS repeat or G/C SNP genotype correlated with histological response or degree of methotrexate stomatitis. Interestingly, presence of the 2R allele was significantly related to relapse ($p=0.01$) but may reflect small patient numbers. Recurrent methotrexate stomatitis (>2 episodes of CTCAE grade 2) was weakly correlated with no relapse ($p=0.07$). Analysis of SNP array data with emphasis on MAP pathway polymorphisms will be presented when complete.

7.P.30

MODIFIED PROLONGED INTRAARTERIAL CHEMOTHERAPY IN COMPLEX TREATMENT PATIENTS WITH OSTEOGENE SARCOMA OF LOWER EXTREMITIES

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In 36 patients was carried out short-lived hyperglycemia and local hyperthermic prolonged intra-arterial chemotherapy on the background of modificators of short-lived hyperglycemia in the department of general oncology of R. O.S. C of the H.M of the Republic of Uzbekistan. Tumour has localized in distal part of femoral bones in 18 patients, in proximal part of cannon bones in 13. Treatment was carried out by the scheme of Syclophosphan 1000 mg/m2 doxorubicin 90 mg/m2 48-hourly unbroken infusion, cycplatin 100 mg^2 in the dependence from efficacy of the treatment has been carried out from 1 to 4 courses In 3-4 hours time after beginning prolonged intraarterial chemotherapy unbrokenly began short-lived hyperglycemia by the way of introduction i/v solution of glucose 20% to1500ml. Maximal concentration of the blood sugar level has composed 18-23ml in the period of treatment. Then local hyperthermia with USD apparatus was carried out in 30MG frequency regime with exposition of 20 min. time. Control group of the patients has composed patients, who has performed system chemotherapy by analogical scheme CAP (in 34 patients). In the patients group, who received prolonged intraarterial chemotherapy with modificators (short-lived hyperglycemia with local hyperthermia) in 4 (11, 1%) patients have been observed full effect, in 25 patients (69, 4%) partial effect, in 5 (13,9%) stabilization, and in 2 (5,6%) progressing of tumour process. Safe operation was performed in 17 patients (47, 2%), crippling in 4 (11,4%) patients, conservative treatment in 15 patients (41,6%) in this group. In patients, who was carried out system chemotherapy full effect was marked in 2 (5,9%) patients, partial effect in 8 (23,5%), stabilization in 15 (44,1%) and progressing in 9 (26,5%) patients. Safe operations were carried out in 3 (8,8%), crippling operations in 19 (55,9%), other 12 (35,3%) patients are under observation after conducting 9 courses of chemotherapy and beam therapy without operation in conservative treatment.

Endovascular chemotherapy in combination with local hyperthermia and short – lived hyperglycemia allows overcoming medicinal steadiness and increases quantity of safe operations. That's why combination prolonged intraarterial chemotherapy with modifications is aimed.

7.P.31

P53 IMPORTANCE IN THE DETERMINATION OF MEDICAMENTAL RESISTANCE OF OSTEOGENOUS SARCOMA OF LOWER EXTREMITIES LONG BONES IN CHILDREN

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It has been determined the prognostic importance of P-53 suppressor in 26 patients with osteogenous sarcoma of long tubular bones of lower extremities. Tumour localized in femoral bone in 14 observations (53,9%), in shin bone-11 (42,2%) and in fibular bone-1 (3,9%).
According to methods of treatment, all patients were divided into two groups:
I group – 18 patients received chemical and beam therapy. Treatment in this group was carried out by following scheme: intraneous metrotrexat, 25 mg/kg for 24 hours with leucovorin, intraneous cisplatin, 100 mg/m² for 4 hours. OOD-2,2Gy, SOD 60Gy beam therapy (telegammatherapy) was conducted after 4 courses of chemotherapy, 5 courses of chemotherapy by above-mentioned scheme was made after the end of beam therapy course.
II group - 8 patients received chemo-beam therapy + operation + chemotherapy by scheme: intraneous doxorubicine, 60 mg/m² for 48 hours, cisplatin, 100 mg/m² for 4 hours on the 3 day, 4 courses with the interval of 3 weeks. After 4 courses of chemotherapy ROD -2,2Gy, SOD 60Gy beam therapy was made. Subsequently after operation 5 patients received 5 courses of adjuvant chemotherapy.
Of 26 patients in 2 (7,8%) was noted complete effect, in 16 (61,5%) - partially effect, in 2 (7,8%) – stabilization of the process and in 6 (22,9%) - tumour progressing.
To estimate study results and determination of medicamental resistance of sarcoma there studied the rates of P-53 suppressor, as study results showed, in 6 (23%) observed moderate or high P-53 suppressor expression in tumor cells, and in 20 (77%) cases did negative and low-positive tumor or low negative and immunohistochemical tumor response. There established that low rates of P-53 suppressor correlated with high sensitivity of tumor to chemo-beam therapy, otherwise there obtained reverse reaction.
Conclusions: study results showed that P-53 suppressor rates have a significant importance in the determination of treatment strategy, tumor sensitivity to chemo-beam therapy and clinical outcome.

7.P.32

PILOT STUDY RESULTS OF COMBINE HdMTX AND ADM/CDDP POLICHEMOTHERAPY TRIAL FOR OSTEOSARCOMA IN POLISH NATIONAL REFERENCE CENTER: SINGLE CENTER EXPERIENCE

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Tempting results of preliminary reports from EURAMOS-1 Study Group and our willingness to join the Consortium were the reason why we decided to start the pilot study exploit EURAMOS-1 protocol (approved by Local Ethical Commission). Since November 2006, 41 patients were enrolled into study (20F/21M, mean age: 14, SD: 3,02) but 1 adolescent refused the treatment at all in 2nd week on. The main localization was thigh (20/41, 49%), followed by tibia (15/41, 37%), fibula (3/41, 7%) and humerus (3/41, 7%). Majority of them had localized disease (27/41, 66%), whereas in 34% (14/41) lung metastases (LM) were revealed at diagnosis. Out of 40, 35 underwent surgery (2 amputations, 33 endoprosthesis) in 11th protocol week as average (mean: 12, SD: 2.80). Among the remaining 5 children, 4 progressed yet during neo-adjuvant CHT and 1 had to finish because of MTX intolerance. Up to now HP examination were completed in 29 children and the median of 12% of viable tumor cells remains (mean: 13%, SD: 22.32%; min. <1%, max. 90%). Fourteen (48%) good responders continued
on MAP arm. Children in whom poor HP response has been confirmed as well as all children with LM, received chemotherapy according to MAPIE arm. The switch between MAP and MAPIE proceeded in 18th week of protocol in average (median: 17th; nim. 14th, max. 24th week). Up to date, in 5 out of 21 patients completed the protocol, the treatment had to be finished untimely because of toxicity and further 5 required CHT switch because of progression. Comparing achieved HP responses with previous experiences, we found no statistically significant differences in rate of tumor necrosis in current study (48%) as in previously used regimens (EORTC 49% and SFOP 44%; OR{EURAMOS/EORTC}=0.96; OR {EURAMOS/SFOP}=1.17; chi-square=0.343 , p=0.842), but the general remarks from the pilot justify study’s continuation.

7.P.33

INTRACORTICAL OSTEOSARCOMA OF THE ULNA IN A 41-YEAR OLD WOMEN – CASE REPORT

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Intracortical osteosarcoma is a comparatively rare and distinct tumor separated from conventional osteosarcoma and other osteosarcoma variants. At first, the lesion was described in two patients by Jaffe in 1960.To date, 17 cases have been described in the literature. In all cases, the tumor occured in the cortex of the shaft of the femur or tibia. En-bloc resection was performed as primary therapeutic approach in most cases, sometimes in combination with neoadjuvant or adjuvant chemotherapy.
We, for the first time, describe a case of intracortical osteosarcoma of the midshaft of the right ulna which was found accidentaly in a patient taking part in a screening programm for heriditary breast cancer.
The patient underwent en-bloc resection without additional chemotherpapy and shows no reccurence after 18-months follow up.

7.P.34

SPINDLE CELL SARCOMA OF BONE – LONG TERM OUTCOMES

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Of 3000 patients diagnosed with primary malignant bone tumours and treated at our unit over the past 25 years, 234 (7.8%) were considered to be spindle cell sarcomas of bone (ie not osteosarcoma, chondrosarcoma, Ewing's, chordoma or adamantinoma). We have analyzed their management and outcomes.
The diagnosis of these cases varied with fluctuations in the popularity of conditions such as MFH, fibrosarcoma and leiomyosarcoma with the passage of time. Treatment was with chemotherapy and surgery whenever possible. 36 patients had metastases at diagnosis and 17 had palliative treatment only because of age or infirmity. The most common site was the femur followed by the tibia, pelvis and humerus. The mean age was 45 and the mean tumour size 10.2cm at diagnosis. 25% of patients presented with a pathological fracture. Chemotherapy was used in 70% of patients the most common regime being cisplatin and doxorubicin. 35% of patients having neoadjuvant chemotherapy had a good (>90% necrosis) response. The amputation rate was 22% and was higher in patients presenting with a fracture and in older patients not having chemotherapy.
With a mean follow up of 8 years the overall survival was 64% at 5 yrs and 58% at 10 yrs. Adverse prognostic factors included the need for amputation, older age and poor response to chemotherapy as well as a pathological fracture at presentation. The few patients with angiosarcoma fared badly but there was no difference in outcomes between patients with other diagnoses.
We conclude that patients with spindle cell sarcomas should be treated similarly to patients with osteosarcoma and can expect comparable outcomes. The histological diagnosis does not appear to predict behaviour.

7.P.35

CHARACTERIZATION OF HLA-A*0201 RESTRICTED CYTOTOXIC CD8$^+$ T CELLS DIRECTED AGAINST EWING TUMOR SPECIFIC ANTIGENS

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The rationale of adoptive T cell therapy is based on the attempt to circumvent pre-existing tolerance mechanisms by stimulating potentially tumor-reactive T cells ex vivo. Efforts to eradicate cancer by adoptive T cell transfer have been limited due to the difficulty of isolating tumor-reactive T cells present in low numbers in peripheral blood of tumor patients. Furthermore, the development of an effective immunotherapy in the autologous context is hampered by the deficit of an effective T cell repertoire against tumor antigens.
We have optimized the techniques for isolating and expanding antigen-specific allogeneic T cells. Following repetitive peptide-driven stimulations with HLA-A*0201 positive dendritic cells the responding HLA-A*0201 negative CD8$^+$ T cells were stained with HLA-A*0201/peptide pentamers. Multimer-positive T cells were sorted and directly cloned by limiting dilution. Using this technique we have succeeded in establishing T cell clones directed against several HLA-A*0201-resticted peptides derived from Ewing Tumor (ET) specific antigens identified via previous DNA microarray analysis and supposed to play a central role in the pathogenesis of this tumor. These T cells not only specifically recognized peptide-pulsed target cells or antigen transfected cells in the context of HLA-A*0201 but also killed HLA-A*0201$^+$ ET expressing the antigen while HLA-A*0201$^-$ ET were not affected.
Allogeneic, tumor specific T cells can be easily isolated via Peptide/HLA-multimer technology and may benefit therapeutic strategies in allogeneic stem cell transplantation.

7.P.36

NOVEL FUNCTIONAL SP1 BINDING SITES IN EGFR GENE INTRON 1

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Tumorgenesis is often accompanied by transcriptional deregulation of oncogenes, such as the Epidermal Growth Factor Receptor (EGFR). Transcriptional activation of a gene requires the binding of transcription factors (TF) to regulatory DNA elements at specific transcription binding sites (TFBS). A better understanding of these interactions and regulation mechanisms is essential for the development of improved therapeutic applications.
ChIP was carried out to prove the existence of four new SP1 binding sites within intron 1 of the egfr gene. Site-directed Mutagenesis was performed on plasmids carrying the regulative sequence of the egfr gene in order to alter these binding sites. Activity of these sites and their influence on the transcriptional regulation were analysed by in vitro transcription and quantification using Ribonuclease Protection Assay (RPA) and qRT PCR.
Using ChIP, four novel SP1 binding sites could be confirmed to be active at the egfr gene intron 1 locus. Expression of the egfr gene was found to be highly dependent of these sites. Consequently, their mutation led to a 50% decrease of the transcriptional activity of the egfr gene.
The four new SP1 binding sites in the egfr intron 1 have a functional role in the egfr gene regulation, leading to a higher transcription rate. As so far only little is known about egfr gene activation, more TFs and TFBSs have to be analysed in order to gain a comprehensive understanding about the regulation of this important oncogene.

7.P.37

MOLECULAR METHODS APPLIED TO ARCHIVAL PARAFFIN-EMBEDDED SAMPLES OF EWING'S FAMILY TUMOURS (EFT)

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Ewing sarcoma is a malignant bone tumour characterized, in 90% of the cases, by the balanced chromosomal translocation t(11;22) which generates a chimeric oncogene that acts as a transcriptional activator. The detection of translocation can be fundamental in cases with an extraosseous or unusual location which are histologically difficult to diagnose and it is also helpful in evaluation of residual disease. We joined immunohistochemical analysis and routine RT-PCR method together, the latter one allowing the detection of the most common fusion transcript EWS-FLI1 in archival paraffine-embedded tissues of EFT patients. We used a pair of primers which allowed us to discriminate between two subtypes of EWS-FLI1 transcript. We selected some sample for EWS-FLI1 typing using a Real-Time PCR assay.
We analysed 54 EFT patients. RNA was extracted from paraffine-embedded sections and reverse transcribed into cDNA. On every sample we performed RT-PCR and immunohistochemistry for the marker CD99; we also selected 5 samples for Real-Time PCR analysis.

Fourty-nine out of 54 samples had a RNA suitable for analysis. Thirty-six patients had EWS-FLI1 type I fusion transcript while 6 patients EWS-FLI1 type II; in 7 samples we couldn't find any fusion transcript although their RNA was good. We tested 5 of these negative samples with Real-Time PCR and we found 2 patients who were carriers of EWS-FLI1 type I fusion transcript. CD99 resulted positive in 34 samples out of 54.
The detection of fusion transcripts using RT-PCR methods can be useful as a support to EFT diagnosis. Moreover the possibility to assess a Real-Time PCR assay enhances analysis sensibility and minimizes the chance of false positives. EFT cytogenetic characterization completes morphologic and immunophenotipic data allowing a more careful classification and an identification of subgroups with different prognosis.

7.P.38

EZH2 IS A MEDIATOR OF EWS/FLI1 DRIVEN TUMOR GROWTH AND METASTASIS BLOCKING ENDOTHELIAL AND NEURO-ECTODERMAL DIFFERENTIATION

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Ewing Tumors (ET) are highly malignant, localized in bone or soft tissue and are molecularly defined by ews/ets translocations. DNA microarray analysis revealed a relationship of ET to both endothelium and fetal neural crest. We identified expression of histone methyl-transferase Enhancer of Zeste, Drosophila, Homolog 2 (EZH2) to be increased in ET. EZH2's suppressive activity maintains stemness in normal and malignant cells.
Here, we found EWS/FLI1 bound to the EZH2 promoter *in vivo* and induced EZH2 expression in ET and mesenchymal stem cells. Down-regulation of EZH2 by RNA interference in ET suppressed oncogenic transformation by inhibiting clonogenicity *in vitro*. Similarly, tumor development and metastasis was suppressed in immunodeficient $Rag2^{-/-}{}_{c}{}^{-/-}$ mice. EZH2-mediated gene silencing was shown to be dependent on histone deacetylase (HDAC) activity. Subsequent microarray analysis of EZH2 knock down, HDAC-inhibitor treatment and confirmation in independent assays revealed an undifferentiated phenotype maintained by EZH2 in ET. EZH2 regulated stemness genes such as nerve growth factor receptor (NGFR) as well as genes involved in neuroectodermal and endothelial differentiation (EMP1, EPHB2, GFAP, GAP43).
These data suggest that EZH2 might play a central role in Ewing Tumor pathology by shaping the oncogenicity and stem cell phenotype of this tumor.

7.P.39

A VARIANT EWING SARCOMA: NOVEL TRANSLOCATION INVOLVING THE NFATC2 GENE IN MULTIPLE CASES

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Ewing sarcoma (ES) is an aggressive sarcoma, and is the second most common bone sarcoma in childhood. Disease specific t(11;22)(~85-90%), t(21;22)(~5-10%), or rarer variant translocations with the involvement of chromosome 22 (~5%) are present. At the gene level, the EWSR1 gene fuses with FLI1, ERG or other ETS transcription factor family members. So far, no ES has been identified with a fusion to transcription factors other than ETS.
By using a panel of molecular tools such as multicolor FISH and array-CGH, a ring chromosome containing chromosomes 20 and 22 was identified in four ES cases. Molecular karyotyping showed the translocation and amplification of regions of chromosomes 20q13 and 22q12. Cloning of the breakpoint showed an in-frame fusion between the EWSR1 and NFATc2 genes. The translocation led to the loss of the N-terminal, calcineurin-dependent control region. Consequently, the remaining intact DNA binding domain of NFATc2 is under control of the EWSR1 promoter region permitting oncogenic activation. Intriguingly, in all cases a distinct histological feature was observed.
In conclusion: a new translocation involving EWS and NFATc2 was cloned that is associated with a histological variant of ES. The NFATc2 transcription factor is not a member of the ETS family of transcription factors. NFTAC2 has well characterized functions in T-cell differentiation and immune response. For the first time a direct involvement of NFATc2 in oncogenesis has been shown.

7.P.40

TO THE QUESTION OF OPTIMIZATION OF TREATMENT OF MALIGNANT FIBROHISTIOCYTIC TUMOR OF SOFT TISSUES

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Aim of the research: generalization and optimization of methods of treatment of patient`s with fibrohistiocytic tumor of soft tissues.
Materials and methods: There were 79 (100%) patients under observation with malignant fibrohistiocytic tumor of soft tissue in the period from 2000 to 2006 year. There were 41 (51,9%) male and 38 (48,1%) female patients. The average age of patients were 45,5. Depending on localization of tumor on the lower extremities 47 (59,4%),on the upper extremities 19 (24%), trunk 13 (16,5%) of patients. Depending on histological structure of tumor the patients were distributed in the following way: 69 (87,3%) malignant fibrous histiocytoma, 10 (12,6%) atypical fibroxanthoma. In 49 (6,2%) cases were the initial tumor, at 30 (37%) were relapse tumor. In diagnostic used complex methods with including into investigation rentgenography, echography, USM, KT and MRT and morphological methods of research. The main methods of treatment are surgical, combine and complex. In initial and localized processes (the size of tumor <5 cm) the main method is surgical (wide carving of tumor). The additional treatments to these patients did not make and they released under dynamic control. In our case there were 24 (30,4%) such kind of patients. In size of tumor from 5 to 10cm, and also in relapse at 17 (21,5%) patients on the first stage made surgical intervention, and then got distance gamma therapy (SOD 50Gy). In postoperative period conducted chemotherapy to 6 (7,5%) patients. In size of tumor more than 10cm in localization in upper extremities and trunk at 5(6,3%) patients the treatment begins with RT, and then surgical intervention +PXT by diagram CAPO, MAID, CAV II and others. In localization on lower extremities at 3 (3,8%) patients treatment begins with intra-arterial infusion Doxorubicin hydrochloride in 30mg/m^2 during for 3 days (90mg/m^2) and then surgical intervention +RT 50 Gy. At 18 (22,8%) patients were carving relapse, at 9 (11,5%) amputation, at 4 (5,1%) patients were exarticulation.

7.P.41

OUTCOME AFTER SURGICAL TREATMENT OF UNDIFFERENTIATED PLEOMORPHIC OR NOT OTHERWISE SPECIFIED (NOS) SARCOMAS OF THE EXTREMITIES-AN ANALYSIS OF 140 PATIENTS

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Undifferentiated pleomorphic sarcoma/NOS (former pleomorphic and storiform MFH) of the extremities is a common malignant soft tissue tumor in adults. The objective of this study is to determine prognostic factors for the outcome after surgical treatment with respect to the recent developments in classification. From 1996 to 2004, 140 undifferentiated pleomorphic sarcomas/NOS were identified out of 1200 soft tissue sarcomas of the extremities that were treated at our institution and recorded in a prospective database. Overall survival (OS) and isolated local recurrence (ILR) were determined by Kaplan-Meier analysis. All tumors were retrospectively analyzed regarding prognostic factors of the disease, including patient's background (primary or recurrent), histological grade (G2/G3), adjuvant chemotherapy and radiotherapy, size (T1-2) and depth of the tumor, and surgical margins (R0, R1, R2).
In 123 patients, a wide resection was performed (limb sparing surgery). In 9 patients, an amputation was necessary. The overall 5-year survival rate was 72% (median follow-up: 52 months). There was a significant difference between the group presenting with primary tumors (5y survival: 84%, $p<0.05$) and recurrent tumors (5y survival: 62%, $p<0.05$). Isolated local recurrence occurred in 36 patients.
In terms of OS and ILR, primary or recurrence, negative surgical margins, size and grading had a highly significant influence, whereas the site of surgery and adjuvant chemotherapy, adjuvant radiation and tumor depth did not. Prognosis for patients with undifferentiated pleomorphic sarcoma of the extremities depends predominantly on adequate wide resection of the primary tumor.

7.P.42

ANALYSIS OF A 12 YEARS EXPERIENCE OF A MULTIDISCIPLINARY TREATMENT OF SOFT TISSUE SARCOMAS

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Introduction: Soft tissue sarcomas (STS) are rare tumors. A multidisciplinary approach including surgery, chemotherapy and radiation therapy is recommended.
Materials and Methods: In the last 12 years, 249 patients with STS were teated in our Institution. All of them were treted with a multidisciplinary approach using all or some of the previous refered treatments.
Results: The overall local recurrence rate in the group of patients submited to surgery was 25% and this factor was related mostly with contaminated margins. Surgical resections were associted with soft tissue reconstructions when needed.
Radiation therapy was used in both regimens pre and post operativly, chemotherapy was also used in 85% of the patients, and was not dependent of tumor histotype.
23 patients were submited to surgery of lung metastasis.
Survival rates were determined and compared with stage (AJCC), tumor histotype and surgical margins.
Conclusions: Multidisciplinary approach is the recommended treatment for STS.

7.P.43

RESPONSE TO ANTIANGIOGENIC THERAPY WITH TROFOSFAMIDE AND BEVACIZUMAB IN A PATIENT WITH HEAVILY PRE-TREATED MALIGNANT FIBROUS HISTIOCYTOMA. EVALUATION OF RESPONSE VIA F18-PET-CT

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Palliative therapy of Malignant Fibrous Histiocytoma (MFH) is mainly based on conventional chemotherapy using anthracyclines and ifosfamide. Intervals between therapies allow abundant recovery of tumour vasculature. An unspecific antiangiogenic effect of chemotherapy can be induced by continuously administering low doses of drug referred to as Metronomic Chemotherapy (MCT). MCT may be combined with specific VEGF targeting drugs in order to increase the antiangiogenic impact on the tumour.
We report on a 57 y.o. male patient with heavily pre-treated advanced stage MFH. Previous polychemotherapies consisted of 8 cycles EIA in adjuvant setting in 2002, 4 cycles ICE in recurrent situation in 2003 and 6 cycles of Dacarbacine plus Epirubicine in 2006. In 2005 and 2006 radiation therapy of paravertebral tumour lesions was done. In September 2006 the patient was admitted to our hospital with multilocular metastatic progressive disease. Performance status was WHO1. A moderate asymptomatic anthracycline induced cardiomyopathy was detected. The cumulative dosage threshold for anthracyclines had been exceeded before. We initiated oral MCT with Trofosfamide 150 mg pd plus iv. - antiangiogenic therapy with Bevacizumab 5 mg/kg q 2w. Follow up (FU) was done via F18-PET-CT.
First FU after 8 weeks of combined therapy showed metabolic partial remission (PR) (48% decrease in mean Maximum Standard Uptake Valule (SUVmax) of target lesions) and metric stable disease (SD) (5% decrease in sum of diameters according to RECIST criteria). Trofosfamide was tolerated well. Treatment with Bevacizumab had to be stopped after 8 weeks because of symptomatic deterioration of cardiomyopathy (Ejection Fraction now 25%). Trofosfamide was continued as monotherapy. After 8 weeks of Trofosfamide alone PET-CT showed one new lesion indicating progressive disease according to RECIST but persistent metabolic remission of all pre-existing lesions. Bevacizumab then was added again but couldn't stop further tumour progression (FU in March 2007). In summary disease control was achieved for 4 months.
Combined metronomic and antiangiogenic therapy led to disease stabilisation and even metabolic remission measured by F18-PET-CT in a heavily pre-treated patient with soft tissue sarcoma. A pre-existing anthracycline-induced cardiomyopathy deteriorated under treatment with Bevacizumab. Whether response duration could have been prolonged by administering Bevacizumab without interruption remains speculative. The role of PET-CT in early detection of response is still to be determined.

7.P.44

SINGLE CENTER EXPERIENCE IN THE SURGICAL AND ADJUVANT TREATMENT OF PULMONARY METASTASIZED SYNOVIAL SARCOMA

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Synovial sarcoma (SS) is rare but increasingly diagnosed and associated with poor prognosis. Primary surgical resection with wide margins and adjuvant radiation-therapy is considered gold standard in treatment of primary SS. Although (Neo)adjuvant chemo- and radiationtherapy are used in the primary treatment of SS, they are not advocated outside a clinical trial setting. In patients with primary SS and pulmonary metastases, (neo)adjuvant chemotherapy is often added to the treatment protocol but it's effect on overall survival seems limited.
Between 1985 and 2004 33 patients with primary SS were treated in our clinic. Seventeen patients were diagnosed with pulmonary metastases at presentation (9) or during postoperative follow-up (8). Wide resection or focally marginal resection followed by radiotherapy was used as primary treatment for all patients. All primary metastasized patients were treated with adjuvant multi-agent chemotherapy including Isofosfamide. Average survival in this group was 32 months (5 year OS 50%), compared to 60 months in the late metastasized patient-group (2 and 5 year OS 50 and 11%). Wide resection was not related to improved overall survival when compared to marginal margins and additional radiation therapy. In the early metastasized group combined chemo-radiaton therapy provided no significant improvement in overall survival over adjuvant chemotherapy or radiation therapy alone. However additional chemotherapy in the late metastasized group was slightly associated with increased overall survival (5 year OS 0% vs 66%).
Treatment of early pulmonary metastasized SS remains highly dependent of the individual preference of patient and physician. In contrast to the reported prolonged disease free / overall survival of Enneking stage IIA and IIB SS patients, aggressive surgical and chemo- radiation therapy has not yet been associated with improvement of disease free / overall survival in stage III disease. Patients presenting with late pulmonary metastasis might benefit from adjuvant multi-agent chemotherapy treatment.

7.P.45

SYNOVIAL SARCOMA OF THE SHOULDER – CASE REPORT

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Synovial cell sarcoma is one of the most common soft tissue tumours. Prognosis of this tumour is related to initial care. Survival rates have improved in the past 20 years because of treatment with primary radical surgery, along with chemotherapy and radiation.
This case report is about a woman, of 68 years old, with a left shoulder-related pain and mass with about four months. The image study showed a lobulated and irregular mass, with about 12x10x9cm, infiltrating the rotator cuff and glenohumeral joint. The core needle biopsy confirmed the presence of a synovial sarcoma, staged as a T2N0M0.
The treatment started with neo-adjuvant chemotherapy, with a poor response. Then, surgery was performed, with a wide excision of the scapula, proximal humerus and clavicle (type IV of Malawer) without reconstruction. The treatment regime ended with the radiotherapy. Eighteen months after the surgery the patient remains disease-free and a neo-joint is starting to form. At this time the DASH score was 63.8. Despite the flail shoulder function is acceptable.
Conclusion: In such an aggressive tumour, an extensive and multidisciplinary approach is imperative but always with regard to the limb function.

7.P.46

A COMPARISON BETWEEN PRE-OPERATIVE AND EXCISION BIOPSY RESULTS IN CHONDROSARCOMA OF LONG BONES

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Chondrosarcoma is the second most common primary malignant bone tumour. Distinguishing between grades is not necessarily straightforward and may alter the management of the disease. We evaluated the correlation between the pre-operative needle biopsy and excision biopsy histological grading of chondrosarcoma of the femur, tibia and humerus.
A consecutive retrospective series of 100 patients with a histological diagnosis of chondrosarcoma was reviewed. Twenty-one patients were excluded because 20 had only excision biopsy and one had only the pre-operative biopsy on record, thus this series included 79 available cases. In 11 instances, there was a discrepancy in histological grade.
Therefore, there was an 86% (68 out of 79) accuracy rate for pre-operative histological grading of chondrosarcoma, based on needle biopsy. However, the accuracy of the diagnostic biopsy to distinguish low-grade from high-grade was 90% (71 out of 79).

7.P.47

CHONDROSARCOMA OF THE ILIAC (ZONE II/III) – CASE REPORT

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Chondrosarcoma is the second most frequent primary malignant tumour of bone, representing approximately 25% of all primary osseous neoplasms. Chondrosarcomas are a group of tumours with highly diverse features and behavior patterns, ranging from slow-growing non-metastasizing lesions to highly aggressive metastasizing sarcomas. As radio and quimio-resistant tumours, the surgery constitutes the unique chance of cure. Nowadays, besides the curative intention, the reconstructive surgery is also a priority in order to save the limb and optimize the function.
This case report is about a young woman, of 24 years old, with hip-related pain and a large mass in the left pelvis. The imagiologic study showed a large mass of about 8 cm of large diameter, starting at the anterior wall of the acetabulum, involving the pubic arcs and with matrix calcification. The core needle biopsy confirmed the presence of a chondrosarcoma, staged as a IIB of Enneking. Because of its size and localization the limb salvage surgery has been a challenge. The surgery included a broad approach of the left hemipelvis, with wide excision of the tumour, reconstruction of the abdominal wall with a propylene prothesis and reconstruction of the hemipelvis with a "custom-made" prothesis with preservation of the femoral neurovascular bundle. The patient started to walk with total bearing after three months and had a normal gait and a nearly normal life during eleven months. Fifteen months after the surgery lung metastasis and local recurrence were diagnosed and she died six months after.
Conclusion: The surgery is our unique weapon in the "combat" against the chondrosarcoma. The reconstructive surgery must be a concern to give to our patients the best functional result and quality of life.

7.P.48

COMBINED TREATMENT OF CHONDROSARCOMA IN CHILDREN

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The aim of the our study was to analyze prognostic factors characterizing biological behaviour of a tumour and specific features of the patient and to develop rational strategy of the combined treatment of chondrosarcoma (CHS) in children.
Between 1982 and 2008 seventy seven patients with CHS were observed and treated in our center. 38 (49,4%) were male and 39 (50,6%) were female. In all cases the diagnosis was confirmed by histological examination. In cases of high grade/mesenchymal or metastatic (into lungs) CHS we use polychemotherapy consist of alternating courses of CDDP, adriamicin, ifosfamide and etoposide and high-dose methotrexate (8-12 g/m^2). Intensive polychemotherapy allow us to expand indications for limb salvage treatment. Using growing (conventional and non-invasive types) endoprostesis improved the quality of life. 5-years RFS was 75,4±7,8 % (Kaplan-Meier curves, p=0.02). The most significant prognostic factors were grade of histological response, morphological type of tumour and type of polychemotherapy (conventional or intensive)

7.P.49

ENDOTHELIN-EXPRESSION IN CHONDROSARCOMA

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Chondrosarcoma are rare malignant tumors. About the biological characteristics of chondrosarcoma is little-known [2]. Endothelin and its receptors are involved in regulating angiogenesis and metastatic dissemination [1]. The aim of this study is first to identify if chondrosarcoma are expressing endothelin-1 (ET-1) and the endothelin-receptors and thereupon to identify potential molecular markers for new target therapies. Another aim is to determine if endothelin is a prognostic factor in chondrosarcoma.
32 cases were investigated clinically and histopathologically. The expression of vascular endothelial growth factor (VEGF), Endothelin-1 , Endothelin-Receptor-A (ETR-A) and Endothelin-Receptor-B (ETR-B) were determined. All data were analyzed by Fisher's exact test ($p<0,05$). All tumors show an expression of either ET-1, ETR-A or ETR-B. Chondrosarcomas with grade (G) I are mostly expressing less than 10-% ET-1 in cells, Chondrosarcomas G II are expressing in most cases between 10-50% and nearly all Chondrosarcoms G III more than 50%. In addition ET-1-expression is correlating with the histological grading. The patients also show a significant high metastatic dissemination probability at the time when tumor samples present more than 10%-storing ET-1-cells. The intensity of ET-1-expression is correlating with VEGF, which is the most important angiogenetic factor in tumors.
Chondrosarcomas are expressing ET-1, ETR-A and ETR-B. ET-1 seems to play a role in the angiogenesis of chondrosarcoma. Increased expression of ET-1 is accompanied with a high probability of metastatic dissemination. Endothelin receptor antagonists, which are used for example in prostate and breast cancer, can represent a potential therapy for chondrosarcoma [1]. Experiments on animals and clinical studies are required.
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2. Streitbuerger A, Hardes J, Gebert C, Ahrens H, Winkelmann W, Gosheger G. Cartilage tumours of the bone. Diagnosis and Therapy. Orthopade. 2006 Aug;35(8):871-81.

7.P.50

CELECOXIB TREATMENT OF CHONDROSARCOMA IN A XENOGRAFT MOUSE MODEL

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In both Enchondromatosis (EC) and Multiple Osteochondromas (MO), multiple benign cartilaginous tumours occur, which have a severely increased risk of malignant progression. Preventing new tumor formation and malignant progression would benefit the prognosis of these patients. A protective effect of selective Cox-2 inhibitor celecoxib, has been suggested against development and growth of colorectal cancer in familial syndromes. At last year's EMSOS meeting we reported on expression of Cox-2 in 37% (central) - 46% (peripheral) of conventional chondrosarcomas. mRNA levels of EC related tumours were slightly higher than the solitary tumours. Celecoxib treatment of the chondrosarcoma cell lines resulted in a 3 fold decrease of PGE_2 levels already at 5 μM. A significant decrease in proliferation was found at 10 μM in OUMS27 and at 25 μM in SW1353 and CH2879 compared to DMSO For the present study we assessed the (prophylactic) effect of celecoxib on chondrosarcoma growth *in vivo* using a xenograft model of immunoincompetent nude mice which were injected with cell line CH2879 subcutaneously. Tumour volume was measured during 8 weeks. Celecoxib serum levels were determined by HPLC. Expression of proliferation marker Ki-67 and Cox-2 was assessed by IHC.
Our *in vivo* results also showed a beneficial effect of high dose prophylactic celecoxib treatment. Tumour volumes were negatively correlated with celecoxib serum levels (r^2=0.152). However, at the end of pubertal growth of the mice, a catch-up tumour growth was observed, resulting in the absence of differences in tumour volume between control and treatment groups. Accordingly, proliferation marker Ki67 was higher expressed in the treated groups at sacrifice.
This suggests that there is no role for celecoxib in the treatment of adult chondrosarcoma patients. Celecoxib treatment of younger patients, especially to prevent formation of new tumours in EC and OC patients, might be beneficial, however more research is necessary.

7.P.51

SYNERGISTIC INHIBITION OF OSTEOSARCOMA CELL GROWTH BY COMBINATION OF RAD001 (EVEROLIMUS) AND ZOLEDRONIC ACID

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Osteosarcoma is the most frequent malignant primary bone tumors. Despite recent improvements in multi-modal therapy the problem of non-response to mono-chemotherapy remains. Therefore, novel multi-drug combinations targeting various molecular pathways are needed to decrease the emergence of resistance phenomenon and to potentiate the treatment efficacy. In this context, the effects of RAD001, a new orally available mTOR inhibitor was investigated in vitro and in vivo on osteosarcoma proliferation, both alone and in combination with Zoledronic acid (ZOL). The in vitro effects of ZOL and RAD001 were analyzed on human (MG63), rat (OSRGa) and mouse (POS-1 and MOS-J) osteosarcoma cell lines in terms of cell proliferation (XTT assay, manual cell counting, time-lapse microscopy), cell cycle analysis (flow cytometry analysis) and apoptosis (caspase 1, 3 and 8 activity). RAD001 and ZOL inhibit MG63, OSRGA and POS-1 osteosarcoma cell proliferation in a dose- and time-dependent manner without any modification of cell cycle distribution. In contrast, MOS-J cells are resistant to ZOL and RAD001. In all cell lines assessed, combination of RAD001 and ZOL exerts synergistic effect on the inhibition of cell proliferation and induces a significant decrease of P-mTOR, P-4EBP1 and Ras expression with no accumulation of IPP and ApppI. This drug combination has been then investigated in a mouse osteosarcoma model induced by i.m. inoculation of MOS-J cells in C57BL/6J mice. Clinical relevant doses of RAD001 (5 mg/kg) and ZOL (100 μg/kg) alone have no effect on tumor growth in contrast to combination of both drugs which decreases osteosarcoma progression. ZOL (alone or in combination) strongly increases bone formation. The combination of RAD001 with ZOL improves tissue repair as shown by important area of fibrosis into the residual tumor mass. The present work demonstrates the in vitro and in vivo synergistic effect of mTOR (RAD001) and mevalonate (ZOL) pathway inhibitors and suggests that ZOL potentiates RAD001 activity through Ras molecular pathway.

7.P.52

ARE TYROSINE KINASE RECEPTORS GOOD CANDIDATES IN PEDIATRIC OSTEOSARCOMAS FOR TARGETED THERAPIES?

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Despite the recent progress, non-metastatic pediatric osteosarcomas have now a 5-year overall survival (OS) around 75% and the metastatic forms are decreasing to 20-30%. To increase these survival rates, new molecular approaches are on development to understand and highlight new candidates for targeted therapies. Tyrosine kinase receptors (TKR) are one of this target class, where new drugs were especially developped, screening now a large spectrum of TKR. After the demonstration among cancers of TKR's clinical utility as surrogate markers to guide the selection of patients susceptible to respond to these treatments, this success was recently tempered in part because of cancers developping resistance mechanisms to these drugs. A study was conducted to evaluate the interest of these molecular targets among pediatric osteosarcomas.
Materiel and methods: 91 pediatric patients treated homogeneously with the French OS94 protocol were included in this analysis. Allelotyping, real-time quantitative PCR (QPCR), sequencing and immunhistochemistry were performed to analyse the following targets: *EGFR*, *MET*, *PDGFRA*, *KIT* and *ERBB2*.
Results and discussion: Most of these targets were rearranged in more than 45% of the population and mainly deleted. Only 11.4% were amplified at *MET* and 8.6% at *PDGFRA*. By QPCR, *ERBB2* was normal in 78 out of 81 informative patients. Surprinsingly, wild-type KIT protein was amplified in 37%. *EGFR* was rearranged by allelotyping in 48% and QPCR evaluation just started. *MET* amplified subgroup is linked to a worst OS than normal and deleted subgroups ($p=0.04$) whereas *PDGFRA* amplified tumors tend to be significantly linked to a better patient OS ($p=0.08$). Considering all amplified subgroups, no ovelap was found as if an osteosarcoma could only be amplified for one gene. This observation could be considered as a way to increase the potential targeted populations where the use of large spectrum TKR inhibitors would be useful in osteosarcoma treatment.

7.P.53

OSTEOSARCOMA MICROARRAY DATA – CONCEPTS TO PREDICT NETWORKS FROM MULTIPLE TYPES OF MESUREMENTS

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[3]EuroBoNet is a European network to promote research in pathology, biology and genetics of bone tumours and aims to join all forces on this field in Europe. The research program comprises 27 members from 11 European countries. The network is actually looking for clinical cooperations to strengthen case numbers for this rare disease and to promote the translational aspect of the network.

The concept of translational research is always hampered by the problem that most of the disease phenotypes do not have a mono causal origin. Therefore most treatment schemes based on one to three drugs are not really productive for most of the patients even if the patients are carefully selected from the responder group. Here the array techniques has inspired many research groups to develop algorithms deriving interaction networks or regulatory networks from this type of data to better get rid of the complexity of the biochemical interactions. The challenge is to find networks and to select the group of master nodes which might be good targets for a balanced multi-drug treatment. This means not only to measure one data type with array techniques but to join array data from multiple platforms and different data levels. Our goal is to integrate these data types to form networks with a predictive character for osteosarcomas.
The existing web platform CAPweb/VAMP from the Institute Curie is based on a Java web-client and R. This platform is focused on array data analysis and visualisation, can be extended by additional R modules and is therefore an excellent choice to implement further algorithms for data integration and network prediction. We are now establishing algorithms beyond a pure association of effects like permutation procedures for optimal rank orders of effects in a given subset of 16 factors which can be assembled to bigger units and selection procedures of gene expression signals by gene dosage concepts.
The presented approach is sustainable because the platform can be constantly extended and improved. On the other hand this platform is end-user suitable. This is the best way to bring theoretical concepts to the bench scientist. As a consequence translational research will become more real and complex systems more feasible.

7.P.54

PROGNOSTIC RELEVANCE OF GENOMIC ALTERATIONS AND ALLELIC IMBALANCES IN OSTEOSARCOMA

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Despite significant improvements of survival in patients with localized osteosarcoma, about 30-40% of the patients still die on tumor progression or relapse. In order to improve therapeutic outcome we postulate the need for individualized intervention schemes based on biological characteristics of the tumor. Identification of molecular changes important for pathogenesis and tumor progression is complicated by the complex karyotype of the tumor with numerous structural and numerical alterations. Here we describe the use of Affymetrix single nucleotide polymorphism arrays in a genome wide high-resolution approach to assay both loss of heterozygosity and variations in DNA copy numbers in 46 osteosarcoma biopsy samples. We combined established histological response parameters with our genetic findings to predict prognosis.
We found that overall chromosomal changes in osteosarcoma are good predictors of response to chemotherapy and outcome. Analyzing the minimal recurrent regions harbouring chromosomal alterations we expanded our investigations towards identification of gains and losses of chromosomal material and found candidate genes as potential prognostic parameters and therapeutic targets. Identified genomic regions and genes were validated by mRNA-expression studies and correlated with proteom analysis by MALDI Imaging.
Thus, structural chromosomal alterations detected by SNP analysis may serve as a simple but robust parameter to predict response to chemotherapy. The results also indicate that we are able to identify several genomic loci with high potential to predict the outcome of the disease. Furthermore new potential target genes were identified by this genome wide screen.
The project is part of the Translational Sarcoma Research Network (TransSaRNet).

7.P.55

BONE DEVELOPMENT GENE DEREGULATION IS INVOLVED IN HIGH GRADE PEDIATRIC OSTEOSARCOMA ONCOGENESIS AND IN THEIR PROGNOSTIC OUTCOME

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Dysregulation of differentiation genes involved in developmental signaling pathways seems to be a decisive event taking part in the multistep oncogenesis. As high grade osteosarcomas are histologically defined by the presence of malignant osteoblasts producing an osteoid component, we focused in a pediatric cohort, homogeneously treated with the French OS94 protocol, on the genomic status at diagnosis on tumor biopsies of several genes involved in flat and long bone formation.
Material and methods: In 91 pediatric osteosarcomas, allelotyping analysis of *FGFRs*, *TWIST*, *DERMO1*, APC, *MET*, *HGF*, and *SDC2* was done. After DNA extraction of paired blood and tumor samples, each locus was analysed by microsatellites bordering closely on each side the targeted genes. Complementary real-time quantitative PCR of *TWIST*, *FGFRs* and *MET* genes and sequencing of *APC* and *TWIST* were performed to determine gene status.
Results: The allelotyping results support the frequent role of each gene: 53.1% of allelic imbalances (AI) were found in 7p21.2 (*TWIST*), 35.3% in 2q37.3 (*DERMO1*), 38% in 5q21 (*APC*), 42.5% in 7q31 (*MET*), 45.5% in 7q21.1 (*HGF*) and 49% for 8q22 (*SDC2*). *TWIST* and *MET* were mainly deleted and no additional *APC* and *TWIST* mutations were identified. Surprisingly, *FGFR1* to *4* are only abnormal in small subgroups. Significant associations were found combining the presence of *MET* AI to *HGF* abnormalities and the presence of *MET*, *TWIST* and *APC* losses. A worse outcome was significantly linked to the presence of *MET*, *TWIST* and *APC* losses ($p=0.05$, 0.04 and 0.02, respectively) but the subgroup combining *MET* and *HGF* abnormalities seems to have a better survival. No correlations was done with other clinical data.
Conclusion: Several genes involved in normal bone development seem to have a role in osteosarcoma development but also to modulate the prognostic outcome of these pediatric patients.

7.P.56

OF THE EXPRESSION OF CL-2 GENE IN OSTEOGEN SARCOMA

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Background: to study the expression of Bcl-2 gene in osteogen sarcoma of long tubular bones and their effect on the disease prognosis.
Study was conducted in 20 patients with osteogen sarcoma of long tubular bones. Of 20 patients studied in 11 patients tumor was localized in femoral bone, in 6 patients in tibia and in 3 patients in fibula. Slices taken from the tumor in open biopsy were the object of research. Immune-hystochemical research was carried out by the standard technique applying antibodies to cl-2. The assessment response was made by visual simiquantity method: expression absence was-0, weak-1 (+), moderately expressed-2 (++), intensive-3 (+++). 17 patients were given chemoradiotherapy, 3 patients combined treatment (surgical + adjuvant chemotherapy). 12 got intraarterial chemotherapy (72 hours) by regimen (Cyclophosphamide, Adriamycin, Cisplatin) - 4 cycles with three week interval. Then telegammatherapy, single dose 3.5 Gy up to general dose 60-70 Gy was made, later chemotherapy was completed up to 9 cycles at the same regimen. 8 patients were carried out 4 cycles of intra-arterial chemotherapy by regimen (Methotrexate, Cisplatin) with three week interval. Radiotherapy used subsequently (General dose 60-70 Gy) and chemotherapy was reached up to 9 cycles at the same regResearch has shown, that in the most of patients 13/20 (65 %) had moderately positive and low positive expression of cl-2 gene, in 4/20 (20 %) cases reaction was negative and in 3/20 (15 %) cases it was the expression of the given gene that was high. The assessment of treatment efficiency was carried out by WHO recommendation. The whole effect was obtained in 6 patients (30 %), partial in 11 (55 %) and progressing was in 3 (15 %). Most patients who were given the treatment by specific scheme: chemotherapy + radiotherapy + chemotherapy had good parameters in life expectancy, where 6 of 8 patients (75 %) lived without relapse and metastases more than one year. All patients (3) had numerous lung metastases in operation + chemotherapy group of patients.
Aggressive current of tumoral process was characterized with high expression of Bcl-2 gene in tumor tissue. The level of expression cl-2 gene can testify the efficiency of conducted treatment.

7.P.57

ROSETTE-FORMING OSTEOSARCOMA: CASE REPORT AND REVIEW OF THE LITERATURE

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Osteosarcoma shows a variety of histologic patterns. Uncommonly, this tumour has an epithelioid appearance, and the rosette formation is more rarely observed.
We report an unusual case of a 12 year-old girl who was referred to us with pain and a mass around her left shoulder with upper limb motor dysfunction. X-ray showed a pathologic fracture of the proximal humerus. Biopsy was performed. Histologically, the neoplasm is characterized by a small multinodular growth pattern. The tumoral cells have plasmocitoid or epithelioid shape and they are arranged forming rosettes. Sheet-like osteoid deposition was found. Inmunohistochemical studies revealed the tumour to be positive for epithelial membrane antigen (EMA), vimentine, CD-99 and neuron-specific enolasa (NSE).
The rosette-forming osteosarcoma has an aggressive clinical behaviour. The location, clinical features and chemotherapy effect are important prognostic factors. Histological differential diagnosis includes small cell osteosarcoma, metastatic neuroblastoma, PNET and metastatic carcinoma.

7.P.58

TARTRATE-RESISTANT ACID PHOSPHATASE 5B (TRAP-5B) OF OSTEOCLASTS IN A SERUM OF PATIENTS WITH PRIMARY BONE TUMORS

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The aim of the study was to examine TRAP-5b as serum tumor marker for patients with primary malignant bone tumors.
In total 69 patients were included in protocol: 34 - with primary malignant bone tumors - 1st group, 35 - with non-oncologic pathology of bone tissue (12 - with benign bone tumors and 23 - with traumatic bone fractures) – 2nd group and 38 healthy donors – 3rd group. The distribution of patients according age and sex in all groups was similar. The level of TRAP-5b was examined by means of immunoassay method.
The low value (<3,0 U/L) of TRAP-5b was found in 39% cases in 2nd group, in 31% cases of donors in 3rd group and only in 3% cases of patients with malignant bone tumors. High concentrations of TRAP-5b (>6,0 U/L) were found in serum of only one patient from 2nd group and only one donor. At the same time TRAP-5b level more than 6,0 U/L was determined in 35% cases of patients with malignancies. The average TRAP-5b value was: 6,14±0,51 U/L in 1st group, 3,9±0,18 U/L in 2nd and 3,7±0,27 U/L in 3rd group. The marker level was higher in group of patients with osteolytic component of bone destruction, compared with group of patients with mixed type of destruction (7,74±0,73 U/L vs. 4,48±0,92 U/L).

7.P.59

THE USE OF ARTIFICIAL INTELIGENCI FOR PREDICTING THE BIOLOGICAL BEHAVIOR OF BONE TUMORS

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Introduction:The prediction of clinical and biological behavior of bone tumors plays an important role in medical tasks such as diagnosis and treatment planning. Different prognostic factors for bone tumors outcome appear to be significant predictors for making definitive diagnosis. It is well-know that different clinical, radiological and histological characteristics are included in diagnostic process. The most important task for pathologist is to determinate biological behavior. Errors in diagnosis lead to wrong therapy and treatment.
It was reason to determinate scores for tumor diagnostics. Score is usually determinate using classic statistical methods such multivariate logistic regression (MVLR), but new computer tehniks, and models of artificial intelligence take a place in modern scoring systems. Recently, classifications tree analysis (CTA) and artificial neural network (ANN) models have become popular in decision-making and outcome prediction of clinical medicine, especially in oncology. This study compared the levels of accuracy of MVLR, CTA and ANN model for the prediction of bone tumor's biological behavior.
Material and method: Data from patient who had diagnosed bone tumors in Institute of pathology, School of Medicine in the period of 10 years (1995-2004) were used for analysis purposed in the study. In the analyzed date –base were 3689 biopsies with these criteria. About 24% (882 biopsies) were excluded because of missing data about radiological presentation. Consequently, data from 2807 biopsies were used for the analyses
Clinical, radiological, histological characteristics, summary 166 variables were analyzed and used to compare the levels of accuracy for the three methods of scoring.
All data were inserting in Spider 2.0 enterprise date-base who assisted MSSQL server 2000.
For MVLR and CTA we used SPSS 15.0 program with incorporate CTA. There are methods of multivariate analysis that allow for study of simultaneous influence of a series of independed variable on the one depended variable (biological behavior of bone tumors). The ANN model used in this study were feed-forward networks, witch were trained with a back propagation algorithm (NNSYSID- Neural Network Based System Identification Toolbox) situated in the Matlab area.
We compared three models across theirs overall percentages. The best model was one with highest overall percentage.
Results: From all analyzed cases 1590 (56, 6%) were males and 1217 (43, 4%) were females patients with Middle Ages 34, 1 (aged from 0-94 years). Malignant bone tumors (prime and metastatic lesions) were 1339 (47,7%) and benign 1468 (52,3%).
From all (166) characteristics 11 were selected on the bases of a definitive analysis and included into scoring system. From clinical characteristics just age of patient and clinical diagnosis "cyst" were included. Next radiological presentations: Pure osteolysis, osteolysis with cortical destruction, osteolysis with soft tissue mass, mixed lytic and sclerotic lesion was statistically significant for scoring model. Histological presents of fibroblasts, giant cells with hamosiderin pigment in stromal cells and atypical stromal cells, and hondroid stromal production were important for classification. Localization in finger's bone was included in definitive score too.

Three performed scoring models showed wary high overall percentages in prediction biological behavior of bone tumors: MVLR 93, 77%, CTA 88, 2% and ANN 91, 5%. The most informative variable, rang 1 in both models of artificial intelligence was radiological criterion. For CTA it was radiological presents of lytic lesion with soft tissue mass and for ANN was combined lytic and sclerotic presentation.
Conclusions: All three scoring models are very useful in prediction bone's tumor behavior, most of them each ones had priority versus others. The most successive (overall percentage 93, 77%) was MVLR. ANN had high sensitivity (overall percentage 93, 77%) and gave ranges of variables included in score. CTA algorithm had the least overall percentage but it is very simple and figurative for interpretation.

7.P.60

WHAT IS THE RISK OF DEVELOPING A BONE SARCOMA IN PREMALIGANT CONDITIONS?

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Aim: To estimate the risk of bone malignancy arising in premalignant conditions.
Methods: There are quite a number of possible premalignant conditions with considerable uncertainty about the actual risk of a bone sarcoma developing. The incidence of these malignant conditions was identified from a prospective database containing 3000 primary bone sarcomas.
Results: 178 of the 3000 patients with newly diagnosed bone sarcomas had a pre-exiting condition which in all probability led to the sarcoma. These included 50 with previous radiotherapy treatment and 47 with Paget's disease. 31 patients developed malignancy in HME, 8 with neurofibromatosis and 7 each with Ollier's disease and retinoblastoma. There were 4 malignancies in patients with Mafucci's syndrome, 3 in patients with fibrous dysplasia, 3 in patients with synovial chondromatosis and 2 in patients with Rothmund-Thomson syndrome.
Given that the incidence of bone sarcomas is 9/million population per year, our 3000 patients represent 333 million population years. When the incidence of a condition is known in the population this allows an estimation of the risk of malignancy compared with the normal population. Retinoblastoma for instance is known to arise in 1 in 16000 births. The 7 malignancies we saw thus represents a risk to individuals with retinoblastoma of 336/million/yr - a figure 37 times the risk of the normal population. Approximate figures of risk have been calculated for other entities.
Conclusion: Data from a supra-regional register allows an approximate estimate of the increased risk of bone tumours in premalignant conditions.

7.P.61

TUMOURS AROUND THE FOOT, DO YOU RECOGNIZE THEM?

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Bone tumours around the foot are relatively rare. I composed a poster with a short history and some images on seven different tumours around the foot. The reader is asked to give the most likely diagnosis. The answers can be found hidden on the poster.
The aim is to enlarge the knowledge of the EMSOS participants on tumours around the foot.

7.P.62

ISOLATED LUNG PERFUSION (ILuP) WITH MELPHALAN IN PATIENTS WITH PULMONARY METASTASES: PRELIMINARY DATA

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Current 5-year survival after complete resection of pulmonary metastases is ≈30%, and many patients develop pulmonary recurrences. Obviously new treatment options are needed for this indication. Isolated lung perfusion (ILuP) is an experimental technique to deliver high-dose chemotherapy to the lung without systemic exposure. Recently, a phase I trial of ILuP combining 45 mg melphalan followed by pulmonary metastasectomy for resectable lung metastases proved to be feasible and safe.
The current 3-center phase II study (including University Hospital Antwerp/P. van Schil and Anthonius Hospital Nieuwegein/ F. Schramel) allows patients with resectable lung metastases from colorectal cancer, soft tissue- and osteosarcoma to be treated with ILuP prior to metastasecomy.
At Leiden University Medical Center we treated 8 patients: 4 with colorectal cancer (age 54-59 y), 2 osteosarcoma (19-20 y), 1 sarcoma NOS of bone (38 y) and 1 sarcoma NOS (56 y) of soft tissue. The number of metastases was 1-2 and one patient had resection of 9 metastases. The procedure was uncomplicated in 7 cases and 1 patient had reversible pulmonary edema. Hospital admission duration was 6-8 days in the uncomplicated group and 14 days in the one patient with a complication. No long term toxicity was observed with extensive follow-up including lung function tests. With a median follow-up of 7 months (range 2-16), only the patient with 9 metastases had a recurrence and died of disease.
Our single center prelimininary data show that ILuP is feasible and does not lead to irreversible or severe toxicity. Compared to retrospective data with metastasectomy alone, perfusion did not add toxicity. Follow-up is too short to draw any conclusions on efficacy.

7.P.63

OSTEOSARCOMA IN CHILDREN AGED LESS THAN FIVE YEARS AT DIAGNOSIS: EXPERIENCE OF THE COOPERATIVE OSTEOSARCOMA STUDY GROUP

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Background. The incidence of osteosarcoma varies considerably with age and preschool children are extremely rarely affected. This study was conducted to investigate presentation, treatment, and outcome in very young children with osteosarcoma.
Patients and methods. The authors retrospectively analyzed the data of 2706 consecutive COSS patients with newly diagnosed high-grade osteosacroma of bone and identified 28 patients (1.0%) aged less than five years at diagnosis. Demographic, diagnostic, tumor, and treatment related variables; response and survival data of these 28 were analyzed.
Results. Of the 28 (male, N=16; female, N=12) toddlers, 27 presented with high-grade central osteosarcoma of an extremity (femur, N= 12; humerus, N=10; tibia, N=5) and one with a secondary osteosarcoma of the orbit. The size of primary extremity tumors was large (≥1/3 of the involved bone) in 20/27 evaluable patients. Primary metastases were detected in 4 children. All patients received multiagent chemotherapy, and 13/20 analyzed tumors responded well (>90% necrosis) to neoadjuvant chemotherapy. Limb sparing surgery was performed in 11, ablative procedures were performed in 14, and no local surgery was performed in two patients with extremity tumors. With a median follow-up of 3.8 years (6.2 years for survivors), 13 patients were alive (CR1, N=12; CR3, N=1). Four patients never achieved a complete remission and 12 developed recurrences (local, N=3; metastatic, N=8; site unknown, N=1); and 15 of these 16 patients died. Five-year overall and event free survival probabilities were 50% (SE 10%) and 46% (SE 10%). Better survival was correlated with good response to chemotherapy.
Conclusions. Osteosarcoma is extremely rare in preschool children. These young patients often have large tumors which may require mutilating resections. Prognosis may be poorer than in older patients.

7.P.64

OSTEOSARCOMA IN YOUNG CHILDREN: CLINICAL CHARACTERISTICS AND PROGNOSIS.

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Osteosarcoma rarely affects young children. To determine the clinical characteristics and the prognosis of this cancer in children of less than 5 years at diagnosis, we retrospectively analysed medical records of these patients treated in French centers between 1980 and 2007. A centralised histological review was carried out.
Fifteen patients were studied. Long bones were involved in 14 cases. Metastases at diagnosis were observed in 40% of patients. Histologic type was 74% osteoblastic.
In 3 cases (20%) tumours occurred on a particular background (tall constitutional size, treatment with growth hormone and pregnancy induced by clomiphene). One child had a second cancer 13 years after the first diagnosis.
Twelve children received pre-operative chemotherapy including high dose methotrexate: 5 of them had progressive disease; only 36% had good histological response (less than 10% viable cells). Limb salvage surgery was performed in six cases (40%).
Chemotherapy was well tolerated in most patients. A one-year-old child developed a severe late convulsant encephalopathy with lesions of the white substance that could be due to methotrexate despite adjustment of doses to his weight.
The functional recovery of the three analysable children who underwent limb salvage surgery is uneven and shows frequent mechanical or infectious complications (2 to 5 reinterventions per patients).
First complete remission (CR) was obtained in 12 children, six of them relapsed. With a median follow-up of 15 years, six are alive in CR, six died of disease (40%), two were lost to follow-up and one has stable disease with metastasis.
This study shows that osteosarcoma seems to be more aggressive in children under five years of age. Surgical management remains difficult in this population. Prospective studies are still needed to confirm these observations.

7.P.65

OUTLOOK FOR VERY YOUNG CHILDREN WITH PRIMARY MALIGNANT BONE TUMOURS – THE LONDON SARCOMA SERVICE EXPERIENCE 1999-2009

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Medical records of children </=5 years, treated by the London sarcoma service for malignant primary bone tumours (average new cases osteosarcoma (OS)/Ewings sarcoma (ES), all ages: 125/year) between 1999 and 2009, were reviewed.
Results: 5 OS and 6 ES. Mean age – 4.2 years (range 2.1-5.8), 8/11 males. OS primary sites: distal femur (2), proximal femur (1) and proximal humerus (2); localised tumours only. Primary sites in the ES cohort included 1 distal femur, 2 chest wall (1 - spinal extension), 1 buttock (spinal extension), 1 temporal bone and 1 ulna; 1 had bone/bone marrow involvement, 1 had chest metastases. 4/5 OS (Euramos, MRC B007) and 5/6 ES (Euro-Ewings 99) were entered into phase III clinical trials. Delayed surgery for OS occurred at mean 12.1 weeks (range 11 – 13) – 4 limb salvage prostheses with 2/4 non-invasive growers, 1 forequarter amputation. All had a good (>90% necrosis) histologic response to neoadjuvant therapy. Delayed surgery for ES occurred at mean 21.7 weeks (range 12.8 – 35), 1 limb salvage with prosthesis (non-invasive grower), 1 biological reconstruction; remainder had tumour resections. Histologic response: 50% good. In the OS cohort, 1 child died a toxic death; 1 developed pulmonary metastases and died 2 years from diagnosis; 1 has a metastatic recurrence in the opposite humerus 2 years from diagnosis and starts 2nd line therapy; 1 had local recurrence 1 year from diagnosis but alive at 7.4 years;1 alive/disease free at 2.5 years. In the ES cohort 5/6 are alive disease free -1, 4.1, 5.2, 6.9 and 7 years from diagnosis; 2 needed 2nd line therapy for recurrent distant disease 4.5 and 5.8 years off therapy, 1 of whom has just recurred again (6.1 years from diagnosis).
Conclusion- improving early survival rates in the very young with OS remains a significant challenge. Quality of survival requires further age-appropriate study.

7.P.66

SOLITARY SKELETAL RELAPSE IN OSTEOSARCOMA: FINDINGS IN 38 PATIENTS FROM THE COOPERATIVE OSTEOSARCOMA STUDY GROUP (COSS)

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Only few patients with osteosarcoma relapse with solitary skeletal lesions as only sign of recurrence. We used the COSS database to learn more about these rare occurrences.
This report covers all patients with high-grade osteosarcoma of the limbs or axial skeleton registered into the COSS database between 1980 and 2003 who developed 1st recurrences as solitary osseous lesions distant from the primary tumour before 01/2005. Patient-, tumour-, and treatment-related variables and outcomes were ev 38 patients (27 male, 11 female) developed solitary osseous recurrences a median of 2.1 years (range: .5 – 14.3) from primary diagnosis. Primary sites had been limbs in 36 and axial in 2, relapses involved axial sites (24), limbs (10), or craniofacial bones (4). Treatment for osseous recurrence included surgery in 28 patients, radiotherapy in 10, and chemotherapy in 27. After a median follow-up of 1.9 years (range: .1-21.2) from 1st recurrence for all 38 patients and 5.5 years (.3-21.2) for 16 survivors (10 of these in continuous 2nd surgical remission), 2- & 5-year overall and event-free survival probabilities were 55% & 34% and 34% & 27%, respectively. A long interval to recurrence (> 1.5 years) predicted for better outcomes ($p < .01$). For those 21 patients achieving a 2nd complete surgical remission, 2- & 5-year overall and event-free survival probabilities were 81% & 61% and 52% & 49%, respectively, while only 1/17 patients failing to achieve a 2nd complete surgical remission survived beyond 5 years ($p < .001$) after additional radiotherapy. 14/16 survivors had also received 2nd-line chemotherapy.
1st solitary skeletal recurrences of osteosarcoma seem to have a favourable outcome provided treatment includes complete surgery as part of multimodal therapy. Some presumed bone metastases may rather represent second primary osteosarcomas.

The COSS studies that form the basis of this report were supported by Deutsche Krebshilfe.

H O.01

ROTATIONPLASTY: GUIDING PATIENT AND FAMILY DECISION MAKING

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Rotationplasty, or the Van Nes procedure, is a surgical option for reconstruction of the lower extremity after resection of a malignant bone tumor in predominantly skeletally immature patients. The procedure usually involves resection of the femur and knee joint en bloc. Virtually all soft tissues, including skin around the tumor, are excised, and the sciatic nerve is preserved. The vessels can be resected and re-anastamosed or preserved. The leg and foot are rotated 180 degrees and reattached, preserving and/or restoring the nerves and blood supply. The foot and ankle which face posteriorly, then function as a knee joint in a custom-made prosthesis. Although this procedure has been successfully performed for many years, patients and families cite cosmesis as a major consideration when making this decision. The lack of knowledge and understanding of the functionality, the psychosocial adjustment, and the quality of life with the rotationplasty, also, present challenges for families with respect to acceptance of this surgical choice.
Two case studies will be discussed to demonstrate the biopsychosocial elements of this procedure. These two individuals, 2.5 years and 24 years post-rotationplasty respectively, have attained success in their personal and professional lives, and they have willingly and enthusiastically shared their experiences with patients and families considering this surgical option. Using Roy's adaptation model, this presentation will focus on adopting positive role modeling to enhance adaptive strategies needed by patients and families to guide their decision making.

H O.02

LIVING WITH VAN NES ROTATIONPLASTY

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A rotationplasty is a unique surgical procedure used to reconstruct after resection of a tumor of the leg or a congenital defect. This procedure avoids phantom pain, limb length discrepancy and infections or implant related complications. The outcome is unusual for cosmesis but very functional.
Background: Borggreve first described a rotationplasty in Germany in 1930 for a 12 year old patient whose knee was destroyed by tuberculosis. In 1950 Van Nes modified the procedure. Kotz and Saltzer described in 1982 the use of a modified version of a rotationplasty to treat malignant tumors of the distal femur.
Case studies of two such patients will be presented.
A 27 year old man had a non-metastic osteosarcoma of his distal femur at the age of five.
He underwent chemotherapy and a rotationplasty. Six years after his operation a correction osteotomy was done. He is doing very well physically and mentally. He graduated business studies, went yearly on Alpine skiing on two legs, likes jogging and perceives no limitations in his life (MSTS, TESS, SF-36).
A 24 year old man, 14 years after a Ewing-sarcoma of his hip. He underwent chemotherapy and radiation therapy. Thirteen years later he had a pathological fracture after playing soccer. He was treated with a total hip prosthesis without screening the malignancy. However the pathology of the specimen showed a postradiation sarcoma. He underwent a modified Van Nes rotationplasty (knee for hip and ankle for knee).
Although is said that rotationplasty had a poor cosmesis and poor psychosocial acceptance, this is not our experience.

H O.03

DELAY IN THE DIAGNOSIS OF BONE TUMOURS; "SOMETIMES IT'S CANCER CAMPAIGN" TO IMPROVE AWARENESS OF CANCER SYMPTOMS IN THE TEENAGE AND YOUNG ADULT POPULATION

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Cancer is a major health problem for teenagers and young adults (TYA's). However, many young people are often late to receive a cancer diagnosis. Young people may not recognize symptoms as serious and delay seeking help. Furthermore, there is evidence to suggest that once a young person does seek help from a general practitioner (GP), significant delay can still occur.
During the annual Find Your Sense of Tumour (FYSOT) conference 2007; a group of 200 TYA's with cancer participated in a survey regarding their diagnostic experience; the cohort included 22 patients with bone tumours. Following the onset of symptoms; nearly half of the TYA's with a bone tumour (46%) reported 4 or more visits to their G.P before being referred to a specialist. However, 91% of bone tumour patients had multiple, 'classic' cancer symptoms and the majority (77%) sought help from the G.P within 4 weeks of noticing symptoms.
The 'Christie Crew' (CC) are a group of TYA's who have been treated for cancer and work on various projects to improve cancer services. The Christie Crew wanted to empower young people with the knowledge that TYA's do get cancer and to raise awareness of the signs and symptoms of cancer and have produced a DVD and education pack that has been launched across 80 schools and throughout the North West.
The DVD is highlights individual's stories of diagnosis. There is also a poster campaign highlighting signs and symptoms of cancer being displayed in large public venues across the Manchester area. The aim is to roll out the project nationally as part of the health awareness (Healthy Schools) initiative. By highlighting that young people get cancer it is hoped that more young people will recognise the signs and symptoms and be empowered to go to their GP if they have persistent problems.

H O.04

A RETROSPECTIVE STUDY COMPARING INITIAL GP DATA ON TWO WEEK WAIT REFERRALS WITH CLINICAL REVIEW AND IMAGING AT A SPECIALIST CENTRE

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Objectives: Background: In 1999 all General Practitioners (GPs) in the UK were sent guidelines about the criteria for urgent referral of patients with suspected sarcoma. In addition, the receiving specialist centre was given a set of targets to meet in relation to referral, diagnosis and treatment of these cancers. These targets have now been updated for 2008 in the Cancer Reform strategy.
Aim: To compare the clinical information on two-week wait referrals with imaging clinical assessment within a specialist centre to confirm a malignant diagnosis; to review sarcoma diagnosis hit-rate and to establish whether early diagnosis has been improved.
Methods: All two-week wait referrals direct into our department were studied from June 2007 to June 2008 to determine whether a sarcoma was diagnosed, whether the GP criteria were met, and whether the targets were achieved.
Results: A total of 166 referrals received as two-week referrals to the specialist unit. One hundred and thirty six were diagnosed with benign lesions. Thirty patients had a malignant diagnosis and of those 10 patients had surgery as their first definitive treatment.
Conclusions: Detailed analysis is still being undertaken but initial conclusions drawn seem to suggest that there are still a large number of inappropriate referrals being made under the two week wait. This may be due to the GPs not following the criteria on the referral form.

H O.05

UNITED TO BEAT CANCER: PHYSIOTHERAPY AND OCCUPATIONAL THERAPY PROVISION ON THE YOUNG ONCOLOGY UNIT AT THE CHRISTIE FUNDED BY A UNIQUE PARTNERSHIP WITH MANCHESTER UNITED FOOTBALL CLUB

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In 2008 The Christie was chosen by Manchester United Football Club to form a unique partnership. This funded a specialist Physiotherapist and Occupational Therapist to work exclusively on the Young Oncology Unit, creating the first posts of their kind in the UK. The YOU treats patients between 16-24 years old with a diagnosis of cancer, sarcoma being one of the most common in this age group. All patients attending the YOU now receive a fully comprehensive Physiotherapy and Occupational Therapy service to address their rehabilitation needs.

The NICE guidelines (2005) indicate that cancer care for young adults needs to be age specific, age appropriate and undertaken by appropriately trained staff; hence the importance of having specialist therapists on the YOU.

The needs of teenagers and young adults with cancer, both physically and psychologically, are more critical than at any other time in life. During their treatment patients will experience stressful events, such as alopecia, weight loss or gain, altered physical appearance, fatigue, nausea and vomiting, absence from education, and reduced contact with peers. The Physiotherapy and Occupational Therapy roles are essential in enabling young adults to adapt to their diagnosis and learn coping strategies to deal with the stressful events they encounter through their cancer experience.

During this presentation we will describe the unique role of Physiotherapy and Occupational Therapy with teenagers and young adults, using case studies to illustrate the benefits of having dedicated YOU therapists. We will also share with you the innovative ways in which the Manchester United training facilities have been used for different initiatives that have greatly benefitted and motivated our patients and their families. The partnership between two local organisations, one of the biggest football clubs in the world and a world class Cancer Centre has been a unique and positive liaison.

H O.06

THE ROLE OF THE SPECIALIST SARCOMA PHYSIOTHERAPIST IN THE MANAGEMENT OF PATIENTS WITH BONE AND SOFT TISSUE SARCOMA

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The Specialist Sarcoma Physiotherapist aims to ensure that patients with sarcoma receive a coordinated and seamless rehabilitation programme, when and where they need it, to enable them to achieve maximum function and quality of life. The National Institute of Clinical Excellence (NICE) Sarcoma guidelines (NICE 2006), recommend that all patients should have their care supervised by, or in conjunction with a sarcoma Multidisciplinary team (MDT). The role of the specialised physiotherapist on the MDT enables rehabilitation to be provided in a timely and coordinated way (NICE 2006).
Sarcoma and its treatment can have a major effect on the quality of patients' lives. Treatment often involves extensive surgery, coupled with chemotherapy and/or radiotherapy. Rehabilitation of patients with sarcoma is highly specialised. A Specialist Sarcoma Physiotherapy team was set up at The Christie and Manchester Royal Infirmary in 1998. All patients who need it, can access expert rehabilitation and advice. The physiotherapist is a core member of the MDT, attends clinics, MDT meetings and offers seamless rehabilitation to in-patients and out-patients undergoing treatment (surgery, radiotherapy and chemotherapy) for bone or soft tissue sarcoma.
The physiotherapist must have an in-depth understanding of all aspects of sarcoma: treatment modalities, functional and psycho-social issues, and impact of disease progression, etc. Rehabilitation is often intensive and may take months and sometimes years. The physiotherapist will spend many hours with the patient and develops a close relationship where practical as well as emotional advice and counselling become part of the treatment. In the event of metastatic disease, the physiotherapist continues to offer support and helps to maximize independence and function even in the end stages of the disease. Access to specialist advice and rehabilitation helps the patient maximise the benefits of treatment, and aims to improve physical, social and emotional outcomes both during and following treatment.

H O.07

USE OF THE DISTRESS THERMOMETER

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Background: Diagnosis and treatment of cancer are highly stressful for patients. Everyday life is disrupted for the vast majority of patients and their relatives and the cancer experience often results in physical, psychological, social, practical, and spiritual concerns.25% to 40% of cancer survivors continue to suffer from distress.
Goal: To improve the referral to specific professionals.
Intervention: Implementation of the distress thermometer: for the future demand on healthcare, a National Cancer Control Program was developed. Two objectives are the availability and introduction of a validated screening instrument capable of indicating the need for specialized psychosocial assistance and the inclusion of screening for psychosocial problems in the national guidelines for oncologic care. These 2 objectives are in line with the American National Comprehensive Cancer Network (NCCN) practice guideline of distress management. This program introduced the Distress Thermometer (DT), an easily understood, self-reported measure of distress. Patients are asked to rate their overall distress on a visual analogue scale (a thermometer) from 0 (no distress) to 10 (extreme distress).
Implementation: Baseline measurements were done in 2008. In January 2009 we started using the distress thermometer at the orthopedic oncology outpatient clinic. The first results of the baseline measurements and the implementation so far will be presented during the EMSOS 2009.

H O.08

TELEPHONE CONSULT AFTER DISCHARGE

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The orthopedic ward was lacking a moment of evaluation with the patient to discuss the provided care. Also there was insufficient insight in the problems in the home situation after discharge from the hospital.
To solve these problems we started with a nursing discharge protocol. In this protocol we introduced the telephone consult. When a patient knows when he will be dismissed he gets a discharge conversation where he will be informed concerning the telephone consult and gets a short questionnaire. In this questionnaire we ask the patient about there opinion of the provided multidisplinary care in the hospital. A week after discharge the patient will be rang at home to discuss if problems occurred in the homesituation and the questionnaire will be gone through. The data originated from this telephone conversation are processed in a database, so that this information can be used to improve the quality of care.
After half a year we evaluated this telephone consult. Patients experience the personal contact after discharge as valuable, problems are traced early and a number of quality improvements has been carried out as a result of the information from the telephone consult.
The information from the telephone consult is very valuable. It concerns an ongoing process which can be used for fast and effective improvements. The data from the database can also be used for scientific research at multidisciplinary level.

H O.09

NURSE TRANSFER WITHIN THE SARCOMA CHAIN

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University Medical Centre St. Radboud Nijmegen has started the project Continuity of Care and Logistics for adult patients with bone tumors in the spring of 2007 (sarcoma chain). This project is focused on the patient group in a multi professional way. Within this project there also has been looked at the information transfer between different, at the patient involved departments on nursing level.
Transfer between the orthopedic outpatient clinic (gateway specialism for this patient category) and the orthopedic ward goes well, because a nursing pre admitting interview takes place at the outpatient clinic. The report of this interview goes to the orthopedic ward together with the medical chart of the patient.
If the patient is diagnosed with osteo sarcoma or Ewing sarcoma the patient is referred to the department of medical oncology for neo-adjuvant chemotherapy. Between department orthopedics and department medical oncology there is no form of information transfer on nursing level.
To guarantee an improvement of continuity of care for this patient group consultations were held with senior nurses linked to these departments.
From this consultation became clear that there was, however, need for better information exchange.
Since the January 1st 2008 patients who are referred to the department medical oncology by means of the orthopedic outpatient clinic are transferred personally and in writing (copy of the pre admitting report and a summary of the hospitalization for the biopsy) to the nurse coordinator of the medical oncology ward. Because this takes place before the first admittance of the patient on the medical oncology ward it is already clear what the (potential) care problems are. It is also clear how the patient has experienced his sickness process up to that moment and if there are psychosocial problems at hand.
Because of this the nurses who are going to take care of this patient can anticipate and improve their care regarding the personal needs of the patient. Until now not many patients have been transferred this way. This because we have many young patients (children) who go to the children's oncology ward. This department has not participated so far, at nursing level, at this project. Evaluation of this new manner of transfer takes place in March 2009.

H O.10

V.A.C.® THERAPY IN SURGICAL WOUNDS

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Surgical wounds are a problem in bone cancer patients undergoing aggressive orthopedical surgeries, such as hemipelvectomy and hip-disarticulation, which are very aggressive to the tissues. Regarding the wound care, the development of Negative Pressure Wound Therapy (NPWT) has shown to have better results than the standard methods often used in wound care. V.A.C.® Therapy removes fluids and infectious materials, helps protect the wound environment, helps promote perfusion and a moist healing environment and helps draw together wound edges. So, V.A.C.® Therapy has shown to provide cost-effective and clinically proven wound therapy. The aim of our study is to describe nursing care in the management of V.A.C.® Therapy, having in mind the benefits that this therapy will bring to the patient, such as reduced complications, reduced costs and time spent on the ward, helping preparing their discharges.

H P.01

THE ROLE OF A TEENAGE AND YOUNG ADULT ONCOLOGY RESEARCH NURSE IN IMPROVING ACCURAL OF PATIENTS INTO CLINICAL TRIALS

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Improvement in survival for teenagers and young adults (TYAs) has lagged behind those of children and adults, (Stiller et al 2006). In seeking explanations investigators have focused on two main factors. Firstly, the low accrual of TYAs into clinical trials (Newburger et al, 2002), and secondly the lack of appropriate multidisciplinary care (Stevens, 2005).
Data from the UK Office of National Statistics confirms this with 70% of paediatric patients being entered into a clinical trial compared to only 20% of 15-24 year olds. In 2007 the Teenage Cancer Trust (TCT) asked over 200 14-25 year olds with cancer if they had been offered a clinical trial (TCT survey results, 2008). Of the total cohort only 30% reported that they had been given the opportunity to enter a clinical trial. The National Cancer Research Institute (NCRI) established a Teenage and Young Adult Clinical Studies Development Group in 2005 to address the issues surrounding the accrual of TYAs into clinical trials.
At a specialist Teenage Cancer Trust Unit in the UK a TYA Clinical Research Nurse was appointed in May 2008; in order to improve TYA accrual into clinical trials. An audit is currently been undertaken to examine present data of clinical trial entry and retrospective data from 2006 and 2007. The focus of the audit is on patients aged 16-24 years with a bone or soft tissue sarcoma being treated in one TCT unit in the UK.
The audit will examine whether the appointment of a TYA research nurse has influenced the accrual of TYA patients into clinical trials. The paper will focus on the particular difficulties and challenges with recruiting TYA patients and the developing role of the TYA Research Nurse in influencing practice. It is essential that improvements are made with regard to trial entry for this unique age group and the TYA Research Nurse may play a vital role in this in the future.

H P.02

NURSE LED FOLLOW UP CLINICS FOR PATIENTS WITH SARCOMA

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The aim of this audit is to evaluate the patient experience of a nurse led follow up clinic for patients with sarcoma.
Those attending follow up in March 2009 were asked to participate in the audit by completing a short questionnaire. The aim of this questionnaire was to evaluate their clinic experience. It gathered their thought and feelings on being seen by a nurse rather than a doctor and whether they felt that had any implication on their satisfaction with the appointment.
The audit is on-going it is expected that the results will be available for presentation at the EMSOS Nurse Symposium in May 2009.

H P.03

PSYCHOLOGICAL AND SOCIAL IMPACT OF CHONDROSARCOMA GRADE I

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Purpose: Surgery is the only treatment option for chondrosarcoma grade I. Because this cartilage tumour is found by coincidence, patients feel unsafe, are anxious and very emotional. The purpose of this study was to evaluate the psychological and social impact of a chondrosarcoma grade I and to optimize the care of these patients.
Patients and methods: Eighty-two patients with a mean age of 50 years (22 – 80), who underwent surgery because of a chondrosarcoma grade I between 1990 and 2007, participated in this retrospective multi-method study. Assessment followed using, the Short Form-36, the MSTS and a special developed semi-structured questionnaire. The mean follow-up time was 4,8 year. 66 patients had a curettage, fenolisation and bonegraft. Sixteen patients had a resection. Five of them underwent a reconstruction with an allograft and another five a reconstruction with prosthesis.
Results: The majority of the patients (77%) were satisfied with our information. For mortgage and life/health insurance there were consequences in 18% of the patients. The SF-36 displayed slight lower scores in all domains except for mental health. Satisfaction with the operation is connected to emotional acceptance.
Conclusions: For patients afflicted by chondrosarcoma grade I the psychological impact is enormous. Three-quarter of the patients think often about the diagnosis and 40% was concerned about the waiting time before operation. To a lesser extent, patients were concerned about the impact of the chondrosarcoma on their lives. Within both domains, psychological as well social, there is a task for the nurse practitioner or a social worker in improving care of these patients. The extent of the surgical procedure does not influence patient satisfaction. The emotional acceptance of the disease decides the level of patient satisfaction.

H P.04

THE IMPACT OF PATHOLOGICAL FRACTURES ON PATIENTS' QUALITY OF LIFE

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Metastatic bone cancer is a type of bone cancer that occurs more commonly than primary bone cancer. In the development of the disease, pathological fractures can occur, affecting patient's quality of life.
The aim of our study is to describe the impact of pathological fractures in patient's quality of life. This study is based on a retrospective study with 140 patients, who attended the ward of bone and soft tissue tumor unit, regarding the risk of fracture, the nursing intervention and the impact of this type of fractures in patient's quality of life.

H P.05

MEDICAL HONEY – SPECIAL CARE FOR CRITICAL INFECTED WOUNDS AFTER BONE SURGERY

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Wound care is often a problem after bone surgery. There is growing evidence that honey based products demonstrate efficacy in infected wounds after surgery. Honey has antibacterial effects and supports wound healing. Even drug resistant bacteria can be eliminated by the use of medical honey. Honey is easy to use, cost effective and has low side effects.
We report some of our experience in patients with bone tumours after rotationplasty, amputation and other serious surgery.

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