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Problems in diagnosis of bony and cartilaginous lesions of bone

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Lesions of bone with chondroid matrix are a heterogeneous group. The differentiation between a well differentiated chondrosarcoma and an enchondroma can be very difficult. All available clinical, roentenographic, and histological features have to be employed to make the distinction. Histologically, enchondromas of the large bones have well demarcated nodules of cartilage, usually surrounded by attenuated medullary bone. The lesion is relatively hypocellular, and the matrix does not show myxoid changes. Chondrosarcomas tend to be permeative lesions entrapping pre-existing bony trabeculae. The tumor tends to be hypercellular, and the matrix may become myxoid or even liquefied. Of all the histologic features mentioned, permeation of pre-existing structures is probably the single best criterion in differentiating enchondroma from chondrosarcoma. Roentgenographically, enchondromas of the large bones are confined to within the medullar cavity. Erosion or thickening of the cortex is considered evidence of malignancy. This is not the rule in enchondromas of small bones. Just as enchondromas of the small bones can appear histologically malignant, periosteal chondromas, the cartilage associated with chondrodysplasias, soft tissue chondromas and synovial chondromatosis can all have cytological features of malignancy. This points out the importance of correlating the cytological features with the clinical and roentgenographic features when making a diagnosis of a chondrosarcoma.

Most bone forming neoplasms of bone are malignant - osteosarcoma. Osteoid osteomas and osteoblastomas are the benign counterparts. The distinction between an osteoblastoma and an osteosarcoma can be quite difficult. The single best criterion to differentiate an osteoblastoma from and osteosarcoma is permeation of surrounding bone. The diagnosis of osteosarcoma requires that an osteoid or bony matrix be identified, apparently produced by the neoplastic cells. The distinction between a high grade chondrosarcoma and a chondroblastic osteosarcoma may be difficult. Chondroblastic osteosarcomas occur in children whereas chondrosarcomas tend to occur in adult patients. Any significant spindling of the tumor should rule out to the diagnosis of a chondrosarcoma.

There are two types of osteosarcoma which need to be mentioned specifically. Telangiectatic osteosarcoma may be mistaken for an aneurysmal bone cyst. Under low power, both aneurysmal bone cysts and teleangiectatic osteosarcomas show blood-filled spaces separated by septae. In aneurysmal bone cyst, the septae are composed of benign appearing spindle cells whereas in teleangiectatic osteosarcoma, the septae contain highly pleomorphic appearing cells. Hence the only distinction is based on cytology. Low grade osteosarcoma, on the other hand, is an extremely well differentiated neoplasm composed of hypocellular proliferation of spindle cells. The distinction from fibrous dysplasia can be very difficult.

Conclusion. Most chondroid and osteoid producing neoplasms of bone can be diagnosed with great accuracy based on clinical, roentgenographic, and histologic features. A rare case can be extremely difficult to differentiate between a benign and a malignant lesion.

Problems in the diagnosis of osteosarcoma and chondrosarcoma

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There are multiple subgroups and varients in the categories of osteosarcoma and chondrosarcoma of bone. Many of these have important implications in the treatment planning for patients with these tumors. The imaging characteristics of bone tumors are important in the placement of tumors into the appropriate diagnostic category and are an important adjunct to the histology of the lesion.

This presentation will cover the imaging modalities available in the evaluation of these tumors and the role of the radiologist at our institution in the work-up of patients with bone tumors.

Problems associated with placement of tumors into the appropriate subgroup will be discussed. Benign bone and cartilage tumors may present diagnostic problems as well as

metastatic disease to bone and non-tumorous conditions that may simulate osteosarcoma and chondrosarcoma. Examples of these problems and the use of the available imaging modalities will be demonstrated.

Diagnostics and radiologic evaluation of preoperative chemotherapy tumor response in Ewing's and osteosarcoma

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Ewing's and osteosarcomas are by means of imaging diagnosed by help of the age of the patient, site within the skeleton, radiographic appearances and mode of growth inside and outside the bone at MR imaging. In the lack of such characteristics a number of differential diagnostic considerations can be made e.g. intraosseous sclerosing Ewing's and osteosarcoma, chronic or plasma cell osteomyelitis. Parosteal and periosteal osteosarcomas versus myositis ossificans represent a specific challenge. The site of biopsies guided by MR imaging may be decisive for correct diagnosis.

In the assessment of tumor response to chemotherapy, radiography, CT, bone scintigraphy and non-enhanced MR-imaging has a limited sensitivity. Contrast enhanced MR imaging has improved differentiation between responders. Fast dynamic contrast enhanced MR imaging (DMR) has in a few specific studies improved correct prediction of tumor response to 80–90%, but the clinical consequences of this application is unclear. Section limitation, techniques and interpretation of DMR is continuously a matter of discussion and some aspects will be presented in the lecture.

Power Doppler flow imaging has in one study showed promising results in the assessment of tumor response to chemotherapy, enhanced color Doppler is unexplored and the use of dynamic scintigraphy and PET are in progress. For SSG there is a need for a method or a combination of quantitative methods with availability and reproducibility in all centers. Complicated and rare equipment dependent techniques may be adapted in Scandinavia, when their clinical value has been assessed in larger centers in Europe or USA.

Dynamic bone scintigraphy—evaluation of preoperative chemotherapy tumor response in Ewing sarcoma and osteosarcoma

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We investigated patients with Ewing sarcoma and osteosarcoma before and after preoperative chemotherapy according to the SSG IX (Ewing) and SSG VIII (osteosarcoma) protocols. Of 20 patients with Ewing sarcoma 11 were evaluable, 2 patients with rib-tumors had no increase above the background on the dynamic study. Of 17 patients with osteosarcoma 15 were evaluable. According to the ISG/SSG I protocol 5 additional patients will be evaluable until April 98 and reported. 200 scintigrams were obtained during the first 400 seconds after intravenous injection of 7–10 MBq Tc-99m-MDP per kilo body weight. Regions of interest were drawn around the tumor and a reference area, preferably the opposite normal bone, and a time/activity curve was produced. Three criteria on the curves were evaluated: 1. The earliest phase whether an initial "peak" occurred, which was the rule for osteosarcoma preoperatively, but abscent in 2 of the patients with Ewing sarcoma and in the remaining 9 less distinct. 2. The slope of the curve. 3. The tumor to non tumor ratio (T/NT) at the end of the dynamic study. We found:

Change from 1 to 2 investigation, Ewing sarcoma

Histopat response[a]	n	peak disapp.	Curve slope	T/NT decrease (%) median (range)
IV	3	3*	3	62 (65–57)
III	1	1	1	64
II	4	1	2	31 (58–5)
I	3	2	2	35 (48–24)

* normalization of the blood flow/activity

Change from 1 to 2 investigation, osteosarcoma

Histopat response[a]	n	peak disapp.	Curve slope	T/NT decrease (%) median (range)
IV	1	1	1	55
III	9	7	5	41 (59–+11)
II	5	1	0	9 (39–+73)

[a] grading according to the SSG guidelines

Despite that the appearance of the "peak" is less distinct or even missing in Ewing sarcoma compared to osteosarcoma, and the curve slope not to steep, our observations indicate that dynamic bone scintigraphy may contribute to the evaluation of treatment response also in Ewing sarcoma.

Applications of PET in the diagnosis and treatment evaluation of soft tissue sarcomas

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We investigated the value of PET with [^{18}F]-2-fluoro-2-deoxy-D-glucose (FDG) and L-1-[C-11]-tyrosine (TYR) in the diagnosis and treatment evaluation of soft tissue sarcomas.

Patients and methods. 52 patients (mean age 50 (18-75) years, 36 men) suspected of having a soft tissue sarcoma underwent 102 PET sessions. 34 patients received FDG and 18

patients received TYR. In 33 patients the effect of local chemotherapy was studied (in 20 with FDG and in 13 with TYR).

Results. FDG-PET. 6 proved to have a benign lesion and 28 a soft tissue sarcoma. All soft tissue sarcomas were easily identified on the PET images. A difference in metabolic rate of glucose (MRglc) was found between high grade sarcomas and intermediate grade, low grade and benign lesions ($p<.05$). After local chemotherapy the PET images showed an inactive central part of the original tumor, surrounded by an active rim. On histological examination the core of the tumor consisted of necrotic tissue and the rim was the site where either viable tumor tissue was found or an inflammatory reaction was seen. The pretreatment MRglc in patients with a complete response (CR) was significantly higher ($p<.05$) than in patients with a partial response (PR).

TYR-PET. 5 patients proved to have a benign lesion and 13 a soft tissue sarcoma. The soft tissue sarcomas were easily depicted as a hot spot on the PET images. A significant difference in protein synthesis rate (PSR) was found between the malignant and benign lesions ($p<.05$). After treatment the CR tumors showed a decrease in PSR ($p<.05$). 8 PR patients showed 1 or more hot spots after treatment, proven to be viable tumor tissue on histological examination. The 2 remaining PR patients showed negative PET-scans, however their histology showed microscopic islets of viable tumor cells surrounded by extensive necrosis.

Conclusions. Our study demonstrates the ability of PET to analyze tissue biology in vivo. The level of MRglc in FDG-PET provided an indication of the malignancy grade of the tumor. Based on the pretreatment glucose consumption, FDG-PET scanning indicated the tumor response to local chemotherapy, although the lack of specificity of FDG, in terms of differentiation between an inflammatory response and viable tumor tissue, hampered the discrimination between a CR and a PR. In order to avoid the inflammatory signal after treatment, a study with TYR was initiated. Soft tissue sarcomas were clearly visualized with TYR and the calculated PSR of the tumor differentiated between a benign lesion and a malignant one. After treatment a significant decrease in PSR was observed in the CR patients. A hot spot on the post-treatment TYR-PET scan corresponded with viable tumor tissue, indicating the need for residual tumor resection. The absence of a hot spot however was not equivalent with a CR due to the difficulties of detecting microscopic islets of viable tumor cells with PET.

Prosthetic replacements in bone tumors—the long term results

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Limb salvage surgery for bone tumors has been performed at our centre since 1971. It is now possible to review the benefits and complications of this form of treatment.

Patients. Since 1971, we have carried out limb salvage operations with cemented endoprostheses in 878 patients. The primary amputation rate over this time period was 15%.

Results. The complication rate varied greatly both by site and by time. The largest initial problem was with infection of proximal tibial replacements, a rate of 36% decreasing to 12% after 1988 when gastrocnemius muscle flaps were routinely used. Rotational loosening of the hinged Stanmore knee replacement was a problem but appears to have been helped by use of a rotating hinge knee and the use of hydroxyapatite coating at the bone/prosthesis interface. The risks of local recurrence, amputation and revision at 10 years along with mean functional scores are shown below.

	No	Median age	LR	Amp.	Revis. 10yr	Funct.
Prox humerus	82	24	15%	12%	0%	75%
Prox femur	134	44	18%	7%	23%	80%
Distal femur	273	22	14%	7%	50%	84%
Prox tibia	164	20	9%	14%	70%	78%
Pelvis	31	37	26%	16%	20%	68%
Extendable	127	10	12%	9%	100%	80%

Conclusion. Limb salvage using endoprosthetic replacements has advanced considerably in the past 25 years. Patients achieve early functional use of the limb but in young patients complications with time are almost inevitable. With increasing experience these problems can be largely overcome and limb function maintained.

Surgery for metastatic periacetabular destructions

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During 1991–1997 we operated 18 patients with periactabular destructions caused by metastases or myeloma using total hip arthoplasty, augmented with fully threaded rods drilled into the proximal pelvis, as described by Harrington. Patients were examined at 1 week, 6 weeks, 4 months and 1 year postoperatively.

Median survival was 20 (2-84+) months. All patients but 1 were ambulating with support at 1 week. All patients surviving 4 months and 1 year remained ambulating. All but 1 patient reported less pain on weightbearing at 1 week. The results were similar at 4 and 12 months, with all but 1 patient reporting no pain or minor pain on weightbearing. 3 patients with large soft tissue components had varying degrees of neuralgic pain.

1 patient had a single dislocation 1 month postoperatively, another patient had a deep infection. In 1 case where a standard length prosthesis had been used a fracture occurred after one year, leading to reoperation with a longstemmed implant. No cases of implant loosening have been seen.

We conclude that the Harrington procedure is a reliable method of restoring and retaining hip function in cases of

metastatic periacetabular destruction. One of our major concerns is avoiding deep infection as the technique makes revision surgery virtually impossible.

Results from treatment of Giant Cell Tumor—the Scandinavian Sarcoma Group experience

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The contents of the SSG Central Registry concerning GCT is surveyed, and the contributors of data have been asked to supplement missing data. The resulting data file have been analysed.

Patients. 164 patients (mean age at operation 35 (14–76) years, 90 men) are registered, all operated in the period 1986 to 1997. 118 patients were referred virgin to the tumor center, 7 after needle/drill biopsy, 5 after incisional biopsy, and 5 after other procedures. None had metastasis at referral. 28 had a fracture at diagnosis. The location of the tumor was femur in 60, tibia in 35, distal radius in 21, fibula in 11, spine/pelvis/sacrum in 15 cases, and other locations in 20 cases. During the diagnostic work-up, 54 had a needle biopsy, 21 had a drill biosy, 34 had an incisional biopsy and 7 had combinations. 45 were operated without biopsy. 14 had MRI, 46 had CT, and 24 had both. The first operation for tumor was performed in the tumor center in 153 cases, in 6 cases outside the center. 156 had local excision and 1 had an amputation. The surgical margin obtained was intralesional in 95, marginal in 39, wide in 17, and better in 7 cases. The reconstruction used was cementation in 67, allograft in 12, endoprosthesis in 8, none in 14 and other in 18 cases. In 45 cases the information was missing. 142 patients had 1 operation, 12 had 2 operations and 4 had 3 operations for the primary tumor. 2 patients had supplementary radiotheraphy, none had chemotherapy.

Results. The database have currently too much missing data, and the results and conclusions must be considered preliminary. The patients were observed mean 46 (1–130) months. Local recurrence occurred in 26 patients (16%) after mean 15 (1–60) months. 3 had a second recurrence. 90 % of all recurrences occurred within 36 months. 1 patient had metastasis, and was treated by chemotherapy. There was no predictive value of tumor size, margin obtained at first operation, the occurrence of fracture at diagnosis, and Enneking Staging concerning local recurrence. There was no significant difference between those who had reconstruction with cement, and the non cemented, concerning local recurrence. When analysing only those with intralesional margin, the local recurrence rate was higher in the non-cemented group, but not statistically significant. 8 patients have died since the primary treatment, 3 of these from the tumor disease.

Conclusions. The results obtained are not very different from other series. The recurrence rate is in line with the EMSOS study. The follow-up should be at least 3 years to reveal 90 % of the local recurrences.

Osteosarcoma in elderly patients—preliminary report based on the Scandinavian Sarcoma Group Register

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Patients and methods. 68 patients older than 40 years old at diagnosis of osteosarcoma (OS) were reported to the SSG Register. After review of histological slides in 45 cases by the SSG Pathologic Board, 10 patients were excluded (6 GCT, 1 kidney cancer metastases, 1 fibrosarcoma, 1 chordoma, and 1 soft tissue osteosarcoma metastases).

Results. The median age was 58 years at diagnosis, the male/female ratio was 1.2:1 and there were 10 patients with metastases at presentation. The most common locations were femur (17), pelvis (10), and tibia (5) Histological grade was reported as high in 50 cases. Pre- and/or postoperative radiotherapy/chemotherapy was only given occasionally. The 5-year overall survival for 45 patients with high-grade OS was 0.12 (follow-up data was not reported in 5 patients).

Conclusions. The results should be interpreted with caution since the histopathological review is not complete and some clinical data is still missing. We found more pelvic lesions and more patients with metastases at presentation compared to studies of classical OS in children and young adults. Furthermore only few patients had adjuvant chemotherapy. These findings may to a large degree explain why high-grade OS in patients over the age of 40 has a very poor prognosis.

Choice of megaprosthetic reconstruction in bone tumor surgery—inventory of SSG centers

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The use of megaprostheses in the reconstruction of large skeletal defects is an uncommon surgical procedure compared to endoprostheses used in arthrosis, arthritis, or in posttraumatic conditions. The purpose of this study was to investigate what types of megaprostheses are used in Scandinavia at different anatomical locations.

Material and methods. The responsible orthopedic surgeon at all SSG centers in Sweden, Norway, and Finland received a questionnaire. They were asked about type of megaprostheses employed in the reconstruction of the proximal humerus, proximal femur, distal femur, and proximal tibia. The advantages or disadvantages of the megaprostheses were noted.

Results. We have so far received information from 5 centers in Sweden and 2 in Finland. The most commonly used megaprosthesis in the reconstruction of proximal and distal

femur, and proximal tibia was the Kotz (KFTMR). Some centers used the LINK prosthesis. In the proximal humerus, different types of prostheses were used with or without an allograft. The responsible surgeons were satisfied with the function of the employed prostheses but some noted the high prizes.

63 soft tissue sarcomas with two or more local recurrences in the SSG central registry—a preliminary report

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The impact of local recurrence on survival has been a recurrent debate issue in previous SSG meetings regarding soft tissue sarcomas (STS). Many studies show that local recurrence is linked to poor prognosis, regardless of whether it is causative or not. Some patients, however, repeatedly present new local recurrences, but either fail to develop metastases or do so late. This study aims to elucidate if these patients and their tumors have any characteristic features.

Patients and methods. In December 1997 the SSG central registry included approximately 2200 STS. 406 (19%) patients had local recurrences , and 63 (3%) of them (34 male/ 29 female) had had 2 or more local recurrences; 36 patients were reported dead (24 because of tumor, 2 dead with tumor, 5 dead of other causes, and 5 missing info) and of these, 17 had no information on metastasis. Hence, 27 of 63 patients were alive, 5 of which were reported to have metastases (lung 3, lymphglandule 1, and other 1). The remaining 22 patients were of special interest for this study.

Results. Of the 22 patients, there were 16 with no evidence of disease, 5 with disease and 1 with local recurrence. All histologic grades were represented; I (1), II (5), III (7), and IV (6), 3 tumors were not graded, and the histiotypes included malignant fibrous histiocytoma (11), malignant schwannoma (3), epithelioid sarcoma (2), fibrosarcoma (2), and synovial sarcoma, leiomyosarcoma, STS (unclassified), and hemangiosarcoma (one each). The average time from operation until the first local recurrence was 47 (8–96) months, while the time from operation to follow-up averaged 72 (34–100) months. 15 patients had only had surgery once, while 6 had surgery twice. None was registered for 3 or more surgical interventions, probably due to that only the first and last surgeries are listed in the registry (one of the 22 patients was not operated upon).

Future prospects. A detailed multivariate analysis will be performed, including patient and tumor characteristics as well as cytogenetic analyses. It is our belief that elucidating the characteristics of tumors that recur repeatedly locally, but do not give rise to distant metastases (or do so late), will add valuable information to our understanding of soft tissue sarcomas.

Local recurrence in osteosarcoma—the Scandinavian Sarcoma Group protocol VIII

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The local recurrence in relation to surgical procedure and margin was analyzed in patients treated for high-grade osteosarcoma according to the SSG VIII protocol from 1990 to 1997.

Patients and methods. 131 patients were reported to the SSG Register. Surgical procedure and margins have been reported in 125 cases and surgical and pathological reports were retrospectively evaluated in 120. Type of surgical procedure was recorded as local excision (including rotational plasty) or amputation and surgical margins were assessed as adequate, i.e. wide or compartmental, or inadequate, i.e. intralesional, marginal, or contaminated wide.

Results. The local recurrence rate was 6%. 7 local recurrences occurred after local excisions, 4 after a wide and 3 after a marginal excision, and 1 after an amputation. Sites were femur 5, humerus 2, and pelvis 1. The mean time from surgery to local recurrence was 15 (2-31) months. Metastases have been reported in 41/131 patients, among these were 7 patients with local recurrence.

	Adequate margin	Inadequate margin	Total
Local excision	56 (4)	12 (3)	73 (7)
Amputation	50 (1)	2 (0)	52 (1)
Total	106 (5)	14 (3)	125 (8)

Number of patients with local recurrences in parentheses

Conclusion. The rate of local recurrence in SSG VIII study was lower or comparable to other studies. It is clear that a wide or marginal local excision of a high-grade osteosarcoma entails a risk of local recurrence. In this study this risk was 7/73 (10%). Increased effect of the preoperative chemotherapy will reduce the local recurrence rate further. The new ISG/SSG I protocol will hopefully decrease the rate of local recurrence despite increased limb salvage compared to the SSG VIII study (60%).

Metastasectomy and chemotherapy for lung metastases from soft tissue sarcoma—update of the SSG XII trial

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Since July 1, 1996 only 7 patients are randomised from the SSG, 4 patients from Oslo, 1 patient from Lund, 1 patient from Uppsala and 1 patients from Bergen.

The input of patients in this trial has been rather slow. It

has been some problems by approval from the local ethical committees in different countries but this problem is now solved. In a special meeting in Leuven, Belgium, April 17, 1998, between EORTC and SSG it was decided to continue with this trial and activate all SSG and EORTC members to participate.

The content of the protocol will be presented once more during my talk.

Preliminary results of osteosarcoma patients treated according to the ISG/SSG I protocol (pilot study, present study)

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We report the preliminary results achieved in 68 patients (median age 15, (4-35) years; 36 men) with non metastatic osteosarcoma of the extremities treated from July 1995 and March 1997 according to the ISG/SSG pilot study.

Primary treatment conssited of two blocks of HDMTX (metotrexate 12 g/m^2), CDP/ADM (cisplatin 120 mg/m^2; doxorubicin 75 mg/m^2) and HDIFO (ifosfamide 15 g/m^2). Postoperatively, patients were given two (those with >90% tumor necrosis) or three (<90% tumor necrosis) blocks of therapy each consisting of ADM (90 mg/m), HDIFO (15 g/m^2) MTX (12 g/m^2) and CDP (120–150 mg/m^2) G-CSF support was mandatory after cycles with HDIFO and CDP/ADM. No chemotherapy-related deaths were recorded. 55% of the cycles were followed by WHO grade 4 neutropenia and 30% by WHO grade 4 trombocytopenia. Febrile neutropenia developed in one quarter of patients. Transient grade 1 renal toxicity was recorded in 5 patients. 1 patient developed persistent grade 1 renal toxicity with a Franconi-like syndrome. 1 patient had doxorubicin-induced heart failure.

60 patients underwent limb-salvage surgery; 5 were amputated and 3 underwent rotationplasty. 11 patients had complete tumor necrosis, in 34 patients tumors necrosis ranged between 90–99% and 23 patients had <90% tumor necrosis. With a median follow-up of 23 (11–30) months, 56 patients remained continously free of disease and 12 patients relapsed with distant (11) or local (1) recurrence, (actuarial 2-year DFS 76%). On the basis of these results a new ISG/SSG protocol has been activated since March 1997.

One-year nephrotoxicity with the ISG/SSG I protocol

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Objectives. To analyse possible nephrotoxicity in a new protocol for the treatment of high-grade osteosarcoma of the extremities involving a combination of potentially nephrotoxic drugs, i e ifosfamide, cisplatinum and methotrexate.

Patients. Collected from the Rizzoli Institute in Bologna, Italy, and from participating Nordic centres within the SSG-group.

Results. Evaluation of the six-month nephrotoxicity data in September 1997 (24 evaluable patients) showed that 12/24 had a significant affection of the glomerular filtration rate as measured by creatinine-clearance. 19/24 had raised urinary-albumin, a marker for glomerular function, and/or urinary-alpha-1-microglobulin, a marker for proximal tubular function, on one or more occasions. Some of these changes were reversible and others were not at the time of analysis. The significance of this is as yet uncertain. In a pilot study within the ISG/SSG collaboration, only 1/82 patients show signs of nephrotoxicity, persistent reduction of creatinine clearance and mild glucosuria and proteinuria, at follow-up twelve months after treatment (data not presented). The one-year nephrotoxicity results of the ISG/SSG I protocol will be presented at the 24th SSG-meeting in Helsingör in April, 1998.

Dose chemotherapy (HD-CT) followed by peripheral blood stem cell (PBCS) rescue in metastatic and pelvic osteosracoma

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From January 1997 to March 1998 at the Department of Pediatric Oncology of Turin 13 children (6 boys) entered the study. The median age at the time of HD-CT was 13y 8mo (2y 10mo – 17y 3mo). 3 pts had metastases at diagnosis. 10 had metachronous metastases within 30 mo from diagnosis or multiple metastases.

After the preoperative regimen 2 of 3 cases with metastases at diagnosis underwent contemporary resection of primary tumor and metastasectomy; in the other child with vertebral localizations and lung metastases, surgery was not performed.

6 of 10 pts with metachronous metastases were in first relapse at 18–24 mo from diagnosis, 3 in 2nd and 1 in 3rd disease progression. 7 underwent metastasectomy before or after HD-CT.

In 1 pt, who did not achieved the target of CD34+ cell number, a bone marrow harvest was added. All the other cases achieved the required CD 34+ cell number (4.2 – 14.81 x 106/Kg; median 9.5) with 1–6 aphereses (median 2).

Until now 7 pts have undergone 2 courses of HD-CT and 2 cases 1 cycle, for a total of 16 courses; in 4 children the

first transplant is ongoing. Conditioning regimen was well tolerated, also in the case of second transplant. Median time to ANC>500 and PLT >25000 were respectively 10 days (r= 9–14) and 11 days (r= 8–22). RBC and PLT transfusional independence were achieved at day +8 (r= 5–12) and +9 (r= 5–26). Mucositis g.I was observed in 7 courses, g.II in 2. Neither renal nor hepatic toxicity was registered, while fever of 1–5 days occurred after 10 cycles. The median time of hospitalization was 14 days (r= 12–23).

2 pts with metastases at diagnosis are alive in CR at 15 and 18 mo from diagnosis and 1 is alive in VGPR 10 mo from diagnosis. 9 of 10 cases with metachronous metastases are alive (8 in CR and 1 in PR) 1–14 mo from the study entry. The pt with insufficient PBSC harvest, died for progression of disease 6 mo after transplant.

These data show that a single course of CTX + VP16 allows an adequate harvest for two transplants, even in pts heavely pretreated. The conditioning regimen containing Carboplatin and VP16 is well tolerated with mild toxicity, not increased in the second megatherapy course.

A critical retrospective analysis of SSG osteosarcoma trials II and VIII—primary diagnosis and histological response grading

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We compared tumor response after treatment with the SSG II regimen and the SSG VIII regimen.

Patients and methods. 114 patients with osteosarcoma in the extremities had been reported to the SSG II trial and 132 to the SSG VIII trial, respectively. For re-evaluation we have received the histological slides from 93 cases in the SSG II trial and from 121 cases in the SSG VIII trial. Missing data excluded 7 cases in the SSG II trial and 6 cases in the SSG VIII trial and in addition 2 cases with a sarcoma other than osteosarcoma were also excluded from the SSG VIII trial. The response of the tumor to the given chemotherapy was determined from the slides using the following criteria:

Grade I: Little or no identified effect.

Grade II: Areas of acellular tumor osteoid and necrotic and/or fibrotic material, with other areas of histologically viable tumor.

Grade III: Predominant areas of acellular tumor osteoid and necrotic and/or fibrotic material, wth only scattered foci of histologically viable tumor identified.

Grade IV: No histologic evidence of viable tumor identified within the specimen.

Results. In the SSG II material 18 tumors showed grade I response as compared to the 7 tumors in the SSG VIII material. Grade II responses had 52 and 49 tumors respectively. Grade III response was seen in 10 and 43 tumors and grade IV response in 6 and 16 tumors, respectively. The good responders (grade III and IV) encountered 19% in the SSG II material and 51% in the SSG VIII material. The bad responders (grade I and II) were 81% and 49% respectively. The re-evaluation changed the response in 29 cases (25%) in the SSG II material and in 31 cases (23%) in the SSG VIII material. In 9 cases, respectively 10 cases the re-evaluation meant a change from "good responders" to "bad responder".

Conclusion. We found a clear improvement in the response from the SG II to the SSG VIII, but still nearly half of the patients are bad responders (groups I and II). The rate of cases with change in response grade after reevaluation is still too high, around one quarter.

Osteosarcoma study SSG VIII—a preliminary report

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SSG VIII is a prospective phase II study for patients under 40 years with localised high-grade extremity osteosarcoma. From May 1990 to December 1997, 132 patients from 14 Scandinavian centres were registered, of these 119 fulfilled the eligibility criteriae. Median age at diagnosis was 16 (2–39) years and the M/F ratio was74/44 (1.7). The most common tumor sites were the femur (54%), tibia (26%) and humerus (14%). As of March 1998, primary tumor surgery has been reported in 115 patients, of these 58% underwent limb salvage procedures. 6 patients have developed local recurrence (all before 2 years and 4/5 after limb salvage), yielding a projected 5-year local recurrence rate of 6%. Preoperative chemotherapy with 4 courses of high-dose methotrexate (HDMTX) and 2 courses of cisplatin/doxorubicin yielded a good histological response (grade III or IV) in 57%. With a median follow-up for living patients of 43 (1–91) months the projected 5-year metastasis-free and overall survival rates are 61% and 74%, respectively, which appears marginally better than in the preceding SSG II study. The median time to metastases was 16 (1–51) months and 37/38 patients developed their metastases within 3 years. As in SSG II, female sex (p=0.001) and a good histological response (p=0.02) were important prognosticators of a favourable outcome. The sex difference can not be explained by differences in primary tumor response or serum MTX values. Before 1993, patients with grade II response were treated with a continued HDMTX/doxorubicin/cisplatin regimen, whereas they from 1993 were crossed over to etoposide, ifosfamide and G-CSF (VIG). Preliminary data suggest that this "salvage" strategy has failed as there is a trend towards better metastasis-free survival in the HDMTX-based group (p=0.07). 2 patients have died from treatment-related complications; 1 from

acute cardiac dysfunction and 1 from acute myelogenous leukemia.

A critical re-examination of Ewing's sarcoma trial SSG IX—primary diagnosis and histological response grading

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Between 1990 and 1997 104 patients had been reported to SSG IX from 11 Centers. Tumors from 96 patients (1990-1996) have been reevaluated with regard to the primary diagnosis and the histologic response grading of the surgical specimens after preoperative multidrug chemotherapy.

Results. The primary diagnosis. 8 patients were excluded due to the other diagnosis than Ewing's sarcoma. A variable panel of antibodies had been used but CD99 (MIC2) antigen) was applied in fes cases. Electron microscopic examination or cytogenetic analysis was only performed in a few Centers.

Histologic response grading. 52/58 surgical cases were reexamined. 45/52 cases were primarily graded according to Huvos. Reevaluation of response grade was perfromed according to Huvos and Picci. The primary grade (Huvos) was changed in 16/45. The grading according to Picci was easier to apply and more informative than that according to Huvos.

Conclusion. The use of ancillary diagnostics are mandatory in the primary diagnosis and should always be used. The histologic response grading according to Picci should replace grading according to Huvos. Due to the importance of cytogenetic analysis for the primary diagnosis as well as for prognosis, fresh tumor material for cytogenetics should always be saved.

Five-year results of the SSG IX protocol in Ewing´s sarcoma. The Scandinavian Sarcoma Group experience

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The first protocol for Ewing's sarcoma, SSG IV, resulted in a local recurrence rate of 20% and 5-year disease free survival of 43%. In 1990 a new treatment protocol of Ewing´s sarcoma, the SSG IX, was activated by the Scandinavian Sarcoma Group. The protocol features an intensive chemotherapy program of four chemotherapy cycles, each consisting of two VAI (vincristine, adriamycin, ifosfamide) at three weeks interval. Total treatment time is 35 weeks. Local therapy is given at week 9. Inoperable or non-radically operated patients receive hyper-fractionated accelerated radiotherapy 1.5 Gy twice daily between chemotherapy courses to a total dose of 42 to 60 Gy, depending on surgical margin and tumor localisation. The purpose of this novel trial was to improve local control and overall survival.

Patients and methods. 88 patients were included (mean age 20 years, 58 male). The tumor (73M0 and 15 M1) was located as follows: pelvis (18), rib (11), sacrum (9), femur (13), tibia (7), spine (4), scapula (6), fibula (4), foot (4), humerus (3), mandible (2), radius (1), ulna (1), hand (1) and soft-tissue (4). The mean size of the tumor was 10 cm with soft tissue extension in 87%. Irradiation was the local therapy primarily for 43 patients, 17 patients received it postoperatively, 60 patients were operated. The procedure was an amputation in 8 and local excision in 52 patients. The surgical margin was wide in 34 patients, marginal in 10 and intralesional in 3. Histologic response has been evaluated in 57 tumors: 8 G1, 15 G2, 10 G3, 24 G4.

Results. 9 local recurrences have been observed (10%). The estimated 5-year local control is 87%. 24 M0 patients (31%) developed distant metastases. The 5-year DFS was 58% and overall survival 67% for M0 and M1 patients 28 and 27%, respectively. Survival was better in patients with extremity tumors, nonmetastatic tumors, and tumors operated with a wide margin. Furthermore, patients with a total chemotherapy necrosis (G4) had a better DFS than those with a partial (G3) or poor response (G1/2) (p=0.003). The toxicity (WHO) was acceptable (gastrointestinal G1-2; hematological G3-4).

Conclusion. The SSG IX protocol gave better local control and survival rates than the SSG IV. This treatment strategy was very effective for patients with a tumor localised in extremities and without hematogenic metastases.

A critical retrospective analysis of ISG/SSG I osteosarcoma trial primary diagnosis and histological response grading

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38 patients with the histologic diagnosis of grade 4 osteosarcoma have been included in the study. Guidelines for the handling of surgical specimens following preoperative chemotherapy of tumor response were defined.

Chemotherapy response: histological evaluation. With a response to chemotherapy one means that areas of acellular tumor osteoid, necrotic and/or fibrotic material is found. No reponse means unaffected tumor tissue. "Necrosis" means absence of neoplastic cells. They may have disappeared completely or may form "ghost cells" with no preservation of nuclear-cytoplasmic details. Tumor necrosis is followed

by ingrowth of granulation tissue, fibrosis and hemosiderin deposition. Previous experience shows that viable tumor is most likely to persist in the invaded soft tissues, cortex, subcortex, ligaments or around areas of hemorrhage. Note, that osteosarcoma often necrotize spontaneously but not so extensively as in "good responders".

Good responders. Total necrosis, or not more than 10 foci containing not more than 30 cells/focus. Report also whether it is a "total necrosis" (no viable tumor cells) or an "almost total necrosis" (< 10 foci).

Poor responders. All other cases, including those with only one area which is bigger than the focus defined above.

Good responders	Necrosis
9/38 (23.6%)	99–100
Poor responders	Necrosis
29/38 (74.4%)	0–99

The main purpose of the criteria defined by pathologists was: 1) to achieve high standard of interobservers reproducibility, and 2) to define practical rules useful in the objective definition of tumor necrosis.

The initial results along with major problems in the application of the criteria will be reviewed.

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Preliminary results of the pharmocokinetic study in patients treated according to the ISG/SSG I protocol

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The kinetics of Methotrexate, Cisplatin (total and unbound), Adriamycin, Adriamycinol, Ifosfamide and 4-OH-Ifosfamide have been monitored in patients treated according to the ISG/SSG I protocol. In the beginning of February 1998 samples and/or data on 14 courses (3 MTX, 7 CDP1/ADM1 and 4 Ifo) from 5 patients had been obtained. All requested samples were obtained from all these courses except one where the last 3 samples of a CDP1/ADM1 course are missing.

The main problems have been to keep the infusion times stipulated in the protocol without changing the infusion rate and, as a consequence, the adjustment of sampling time. Mostly the initial rate of infusion has been to slow. A request to change sampling times to fit the clinical routine better has also been made. A modified sampling protocol has therefore been produced which also reduces the number of hospitalisation days due to pharmacokinetic sampling. Other slight changes in the sampling procedure are the addition of a "zero" sample before start of Ifosfamide and the possibility of sampling for Adriamycin in plastic vials. The 6 types of analyses performed at three different institutions function well.

Data are still to scarce to allow any conclusions to be drawn. We have however noted that:

1. The desired peak S-MTX level of 1000μM was exceeded without delayed elimination in the 3 courses on which data has been obtained.

2. The induction of Ifosfamide metabolism is pronounced. This was observed as a reduction of the concentrations of Ifosfamide and an increase of 4-OH-Ifosfamide during infusion.

The study continues and more data is needed to relate the kinetics of the cytostatics to their clinical effect.

Preliminary results of determination of P-glycoprotein in osteosarcoma patients treated according to the ISG/SSG I protocol

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Previous studies have shown that P-glycoprotein expression in osteosarcoma samples at the time of diagnosis predicts the clinical outcome. [1-2] These observations do not clearly indicate if the P-glycoprotein status identifies patients who are at a higher risk of relapse, and can therefore be used as a marker to select patients for aggressive therapy. In this study, data on drug resistance at the cellular level will be considered together with information obtained from a concomitant pharmacokinetic study, relating these to the clinical outcome. The expression of P-glycoprotein was analyzed in 20 patients (median age 16; 15 men) with newly diagnosed osteosarcomas, who where considered eligible for the ISG/SSG I protocol for high-grade osteosarcoma of the extremities. 19 cases were from the Istituti Ortopedici Rizzoli, Bologna, Italy, and 1 was from Turku University Central Hospital, Turku, Finland. Tumor samples were obtained before chemotherapy, fixed with buffered formalin and embedded in paraffin. Monoclonal antibodies JSB-1, MRK16, and C494 were used for P-glycoprotein immunodetection. Normal kidney tissue was used as a control. For each specimen, a negative control was obtained by staining the sample with the secondary antibody only, and a positive control was obtained by using a monoclonal antibody for vimentin. The assessement of increased levels of P-glycoprotein was per-

formed as previously described[1].

Results. Of the 20 osteosarcomas 8 were P-glycoprotein negative and 12 had increased levels of P-glycoprotein. Due to a short follow up correlation between the P-glycoprotein levels and clinical outcome was not possible to analyse.

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Detection of microscopic disease in osteosaroma—immunomagnetic isolation of tumor cells present in peripheral blood and bone marrow aspirates

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A small fraction of patients with osteosarcoma (OS) may in fact be cured by surgery only. In contrast, as many as 50% of an unselected cohort of OS-patients die despite aggressive multimodality treatment (1). So far it has not been possible to identify these subgroups of OS patients, and better methods for initial staging and monitoring the effect of chemotherapy are needed. Here we report the results of a pilot study, involving 20 patients at various clinical stages and phases of OS, employing a new method for detecting micrometastatic disease.

The principle is based on the use of "immunobeads" (Dynabeads M450); i.e. paramagnetic monodisperse particles (ø-4.5um) coated with anti-mouse IgG bound onto the Fc region of tumor-associated murine monoclonal antibodies (Mabs). Mononuclear cell suspensions were obtained from samples of heparinized peripheral blood and bone marrow aspirates by Lymphoprep^{R}-gradient centrifugation. Thereafter the cells were incubated with TP-1, TP-3 and 9.2.27 immunobeads, all Mabs that have previously been shown to react with OS cells but not with cells in peripheral blood and bone marrow. Following incubation, bead-rosetting cells were isolated with a strong magnet, and the number of rosettes were counted in a microscope.

All 3 patients with overt metastases at the time of primary diagnosis had numerous rosettes in bone marrow, and one also had rosettes in peripheral blood. In 7 patients, clinically progressing with relapsed metastatic disease, 6 had positive bone marrow samples, 3 of which were positive in peripheral blood. 10 patients with primary tumors, but without known metastases, were examined. 1 with a large inoperable lesion in the maxilla, progressing under chemotherapy and locally treated with external radiotherapy, was positive in bone marrow but negative in blood. In 3 of the other 9 patients under primary treatment, rosettes were neither detected in bone marrow nor in blood. In the remaining patients rosettes were detected at primary diagnosis in bone marrow and in 1 patient also in blood. Interestingly, on repeated examination following preoperative chemotherapy, no rosettes could be found in 5 of the 6 cases. Among 4 healthy donors and 5 patients with non-OS malignancies examined neither had rosettes.

Pitfalls related to confirmation of the malignant phenotype of the isolated rosettes will be discussed. Initial experience employing small fluorescent immunolatex beads (ø-1um) as a "double stain" will be presented. This permits not only tumor cell verification, but can also give important biological information, when tagged with Mabs against multidrug-resistance glycoprotein p-170 or antigens associated with the metastatic process.

Our findings hold promise that this technology may become useful as a diagnostic and prognostic tool in the management of OS.

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POSTER SESSION

Communication with cancer patients in an orthopedic ward

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The aim of the study was to examine the level of information and satisfaction among cancer and shoulder-elbow patients in an orthopedic ward.

Methods. From November 1996 thru May 1997 38 consecutive patients (18 women) with suspected cancer and 38 consecutive patients (23 women) with a shoulder-elbow disease were included. They were matched according to age. The patients in both groups were admitted to the same ward and surrounded by the same staff.. Patients were interviewed the day after the admittance to the ward, again after having received information about the treatment, and finally one month after the discharge.

Results. At admittance to the ward the patients had a low level of information and knowledge regarding examinations and diagnosis and low level of satisfaction. After the first information patients level of information and knowledge regarding examinations, diagnosis and treatment in both groups improved and remained high one month after the discharge. Also patients satisfaction improved and remained high in both groups. There were no differences between the two groups with regard to level of information and satisfaction. Nevertheless, 9/38 patients with suspected cancer, and 12/38 shoulder-elbow patients had a wish for more information on prognosis and rehabilitation.

Conclusion. The level of information and satisfaction were high, and not influenced by the diagnosis of cancer. Despite these findings we found that patients wish for more information regarding prognosis and rehabilitation.

DNA ploidy measurements in bone and soft tissue tumors—a review of approximately 500 cases at the Karolinska Hospital during 1994–1997

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Summary. All malignant and most of the benign bone and soft tissue tumors operated at the Karolinska Hospital are analysed with regard to DNA ploidy and proliferation index. During the last 4 years, approximately 60 such bone tumors and 80 such soft tissue tumors have been analysed per year. Of the bone tumors, more than 50% represent metastases.

DNA ploidy measurements have been performed since 1986. In a pilot evaluation, cell analysis reports from 1994 to 1997 were combined. The data will be presented as a poster.

MRI may be superior to bone scan in the early diagnosis of bone marrow metastases in osteosarcoma

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Clinical history and findings. A 13-year-old girl with an osteosarcoma in the right femur presented with multiple rounded lesions in the bone marrow of the axial skeleton and proximal left femur on pre-treatment MRI, consistent with metastases. Subsequently this was histologically confirmed in one location. A whole body scan performed at the same time was essentially normal. At the completion of preoperative chemotherapy the metastases had regressed on MRI, but showed increased radionuclide uptake, reflecting regressive changes as a response to treatment, the so called flare phenomenon.

Conclusion. The findings suggest that MRI may be superior to bone scan in the early detection of bone marrow metastases, even in a bone forming tumor such as osteosarcoma. This necessitates further studies to establish a suitable protocol for a comprehensive, yet time and cost efficient metastatic survey of the skeleton with MRI in the preoperative assessment of primary malignant bone tumors.

Imaging of glucose utilization and perfusion in osteosarcomas of the extremities by positron emission tomography

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We have investigated glucose metabolism with fluorine- 18 fluorodeoxyglucose (FDG) and blood flow in localized primary osteosarcomas (OS) by positron emission tomography (PET) and evaluated whether these parameters are related to biological behaviour of OS, therapeutic response and MRI finding.

Patients and methods. After an overnight fast, a FDG PET study was performed on 4 patients (age, 16-17 years) with high grade OS (tibia, 3, femur, 1) before therapy (SSG VIII, ISG/SSG I). 2 patients had another FDG PET study after preoperative chemotherapy (CHT), 1 of them also during CHT. Serial blood sampling was performed, and glucose utilization in the tumor was measured as standardised uptake values (SUVs) and regular metabolic rates for FDG (rMR-

$_{FDG}$). Blood flow was measured on 3 untreated patients by PET and oxygen-15 labeled water using one tissue compartment model. Dynamic contrast-enhanced MRI was performed before, during and after the preoperative CHR, and the result were compared with the PET data.

Results. FDG uptake (SUV) in untreated OS was 9.9-18 and rMR_{FDG} 28.8-57.4 µmol/100g/min. Tumor blood flow was 32-52 ml/100g/min. After neoadjuvant CHT tumor SUV decreased 12->4.2>2.1 in a patient with good histopathological response to therapy (grade 3/1-4, SSG VIII), although MRI suggested progression during CHT. Tumor SUV also decreased (18>3.0) in the second patient studied twice, although the histological response was poor (>90% of necrosis, ISG/SSG I). Among those patients studied only once the patient with the lowest SUV and the highest blood flow had a complete histological response (ISG/SSG I), while the tumor with the lowest blood flow clinically seemed to progress and was resected after only one cycle of CHT. The response was poor (90%, ISG/SSG I).

The small number of patients precludes any conclusions, but the study is still ongoing. PET imaging of OS might be used for therapeutic monitoring. The influence of tumor glucose metabolism and blood flow on the final outcome of the patients is not yet known.

The differentiation of osteofibrous dysplasia from adamantinoma of the tibia

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The differentiation between osteofibrous dysplasia from adamantinoma is important for the choice of treatment and outcome. Osteofibrous dysplasia as a congenital anomaly produce a bowing deformity and treatment depends only on the extent of deformity. Adamatinoma as a malignant tumor has to be treated by wide excision to avoid local or distant recurrence. The radiological appearance of both lesions may be identical. Distinction can be made histologically, but requires immunohistochemical staining with cytokeratin.

Patients and methods. We retrospectivelly reviewed 18 patients classified as monostotic fibrous dysplasia (14), intracortical hemangioma (2), and adamantinoma (2) from a 27 year period (1970-1997). All lesions were located in the tibia and/or fibula. The diagnoses were made by consensus by two orthopedic surgeons, two radiologists and two pathologists. We reexamined 6 patients by radiographs and MR-scan of the tibia and fibula, CT-scan of the chest and open biopsy from the persistent intracortical lesions.

Results. After review the diagnoses were: fibrous dysplasia (4), osteofibrous dysplasia (7) and adamantinoma (7). The reexamined patients with an adamantinomous lesion (5) showed no severe progression neither radiologically nor histologically and no dissemination. They were primary classified as intracortical hemangioma and fibrous dysplasia and were treated by curettage and bone grafts. The mean follow up time for the adamantinomas was 11 (3–18) years. We performed one thoracotomy on a young female: the adamantinoma of her tibia had radiologically regressed during pregnancy, while the CT-scan of her chest showed two intrapulmonary nodules. They were excised but found to be benign. We made a new biopsy from her tibia. The histological diagnose was osteofibrous dysplasia. We decided to treat her by wide excision. The mean age of patients with fibrous dysplasia was 30 (18–50) years, with osteofibrous dysplasia 14 (2–50) years and with adamantinoma 10 (5–18) years.

Conclusion. The radiological soap-bubble appearance in the anterior cortex of the tibia, that appears to be pathognomonic for the adamantinoma, may mimic osteofibrous dysplasia. The histological examination with cytokeratin can differentiate the benign from the malignant lesion. It is important, that the open biopsy is not small, because an adamantinomous lesion can show areas without any epithelioid cells, resembling osteofibrous dysplasia.

Fine needle aspiration of osteosarcoma

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Fine needle aspiration cytology (FNAC) may be used in the evaluation of primary malignant bone tumors. The final diagnosis is based on the combined evaluation of clinical and radiographic data and the cytologic examination. High grade osteosarcoma can be diagnosed with (FNAC). Ancillary diagnostic methods performed on aspirates are an important supplement.

47 osteosarcomas were examined by FNAC 1980–1996 and 38 were reported as malignant: 15 as osteosarcoma, 16 as pleomorphic sarcoma suggestive for osteosarcoma, 6 as high grade sarcoma and 1 as malignant tumor. 9 were non-diagnostic: 5 insufficient material and 4 inconclusive with regard to benignity or malignancy. In 10/15 cases with a cytodiagnosis of osteosarcoma definitive treatment was undertaken without histologic biopsy. In 14 of the 15 cases ancillary procedures were performed (combinations of alkaline phosphatase staining, electron microscopic examination and DNA-ploidy analysis).

Results of reexamination. High grade osteosarcoma (osteoblastic, chondroblastic, fibroblastic or mixed) yields reproducible cellular patterns in most fine needle aspirates. Alkaline phosphatase staining and electron microscopy help to exclude a diagnosis of carcinoma and melanoma metastases, large cell anaplastic lymphoma or high grade chondrosarcoma. A non-diploid cell population indicates malignancy and excludes false positive diagnosis in lesions with proliferating osteoblasts.

Conclusion. Combined evaluation of clinical and radiologic data and FNAC supplemented with ancillary diagnostic studies permits a confident diagnosis of high grade osteosarcoma.

Cytological diagnosis of high-grade osteosarcoma

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Patients and methods. In a consecutive series of 44 high-grade OS cases 1990–97, fine-needle aspiration biopsy (FNAB) was done in 41. In 20 cases, most of them from the early 90'ies, the diagnostic work-up was completed with an open biopsy. Thus, a histopathological diagnosis of high-grade OS was obtained preoperatively by open biopsy in only half of the cases.

Results. FNAB was inconclusive in 4 cases necessitating open biopsy. Notably, all these 4 cases lacked the typical clinical and radiological features of classical OS. Even the histopathological specimens from open biopsy posed diagnostic difficulties requiring second opinion by international expertise. In the remaining 37 cases, cytology suggested GCT in 2 patients, low-grade OS in 1 and PNET in 1. However, the 2 "GCT cases" exhibited atypical clinical and radiological features prompting open biopsy. The "low-grade OS" (78-years old) was reclassified after wide excision as a small cell OS. Again, the histopathology of these 3 controversial OS cases had to be confirmed by international expertise. The "PNET case", a 14-years old boy with clinical, radiographical and immunohistochemical findings complying with this diagnosis, was treated preoperatively according to our Ewing´s sarcoma protocol followed by wide local excision. However, histopathological examination of the surgical specimen disclosed an extremely uncommon small cell OS type, i.e. the epithelioid variant, which exhibits not only a similar histologic picture as seen in Ewing´s/PNET, but also the same chromosomal translocation. Overall the cytological diagnosis was correct in all 33 OS cases exhibiting the typical clinical and radiological features.

Conclusions. Our study shows that FNAB is a reliable diagnostic procedure in classical OS. Thus, a cytological finding of markedly atypical osteoblasts and osteoid is sufficient when the clinical and radiological findings suggest classical OS. Open biopsy should be employed in the minority of OS cases exhibiting atypical features with regard to age, tumour site and radiography.

Fine needle aspiration (FNA) of chordoma

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We reexamined 22 aspirates from 18 patients with chordoma. 18 tumors were primary, 3 recurrent and 1 metastatic. There were 14 sacral tumors, 1 lumbal, and 3 from the cervical spine.

20 aspirates were highly cellular, in 1 the yield was moderate and 1 aspirate was non-representative. Tumor micro biopsies, cell clusters and numerous dissociated cells embedded in an abundant myxoid background matrix were seen in all cases. The myxoid matrix characteristically encircled single tumor cells or small clusters of cells. Epithelial-like cells as well as large one-or multivacuolated physaliphorous cells were present in all cases. Spindle cells, single or in tight clusters were observed in 10 aspirates. Gland like structures were seen in 5 tumors. The cell membrane was distinct and bi-or multinucleated cells were a common finding. A marked cellular pleomorphism was observed in a few cases

The most important diagnostic pitfalls were chondrosarcoma, chondroblastic osteosarcoma, metastatic mucusproducing-or clear cell carcinoma and liposarcoma. The typical immunophenotype for chordoma (vimentin, cytokeration and S-100 protein positivity) was helpful in the differential diagnosis.

Conclusion. Chordoma has a characteristic appearance in FNA and a reliable diagnosis can be based on the combined evaluation of clinical and radiological findings and cytomorphology.

Percutaneous transpedicular vertebral biopsy—a routine outpatient procedure

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With the increasing use of MRI more symptomatic and asymptomatic lesions of the spine are found in patients with or without previously known malignancies. Histopathologic diagnosis is essential in such cases. Earlier, different biopsy methods were used. We evaluate the efficacy of percutaneous transpedicular biopsy and its feasibility as an outpatient procedure under local anesthesia.

Patients and methods. 83 consecutive patients who had percutaneous transpedicular biopsies done during 1994–1997 were retrospectively reviewed. Mean age was 59 years. The Osty-cut bone biopsy needle was used under C-arm fluoroscopy guidance.

Results. There were 32 thoracic, 47 lumbal and 4 sacral biopsies. 32 patients had previous malignant disease. Histopathologic examination revealed 15 primary malignancies, 23 metastases, 7 acute/chronic spondylitis (4 tuberculosis), 7 osteoporotic fractures, 7 inflammatory processes/fibrosis, 1 Paget's disease and 22 without abnormalities. One specimen was inconclusive. 53/83 biopsies were outpatient procedures and 58/83 were done under local anesthesia, with increasing numbers performed each year. Complications were minor bleeding (1), transient rhizopathy (2) and headache (1).

Conclusion. Percutaneous transpedicular vertebral biopsy has high diagnostic accuracy (82/83) and very low complication rate (4/83). It can be safely performed as an outpatient procedure under local anesthesia.

The value of FNA in the pre-operative diagnosis of chordomas

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Chordomas are rare tumors of notochordal origin in the spine and skull base. Their metastatic potential is relatively low but the long term prognosis is nevertheless poor due to local recurrences. To avoid or diminish the risk of tumor dissemination, any diagnostic biopsy procedure prior to surgery should be as non-traumatic as possible.

Patients and methods. We have used fine needle aspiration biopsy as a diagnostic procedure in order to minimize biopsy trauma and to allow function preserving-surgery. We report the results of preoperative fine needle biopsy of chordomas in 21 patients; 15 of these were diagnosed solely by fine needle aspiration biopsy.

Results. The typical yield from chordomas was cellular and characterized by groups of cells in a myxoid stroma. The tumor cells were often large and well demarcated. The cytoplasm was pale and often bubbly due to numerous cytoplasmic vacuoles of varying size. The smears also contained smaller epithelial-like cells and spindle cells. The nucleus was usually centrally located with 1–2 small nucleoli. In some cells, however, the nucleus was peripherally compressed and scalloped by vacuoles.

Conclusion. This study shows that it is possible to achieve high diagnostic accuracy with fine needle aspiration biopsy, particularly if immunocytochemical methods are included in the investigation.

Changes in the p16 gene in human chondrosarcomas

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The CDKN2 gene encodes the tumor suppressor protein p16, and has been found altered in many forms of human cancers. p16 functions as a negative regulator in the cell cycle.

Patients and methods. Cells from 10 chondrosarcomas, 10 normal hyaline cartilage biopsies, and lymphocytes from 1 chondrosarcoma patient were analysed. Genomic DNA extracted from cells cultured in monolayer were used for amplification by PCR. Exons 1, 2 and 3 and their flanking regions of introns of the CDKN2 gene were amplified. An amplified fragment of the gyceraldehyde-3-phosphate dehydrogenase gene was used as a positive control. The amplified fragments of exons 1 and 2 were subjected to sequencing.

Results. All 3 exons of CDKN2 were deleted in 3 of the chondrosarcomas. All samples of normal chondrocytes and the lymphocyte sample contained all exons. 1 chondrosarcoma contained a heterozygous substitution (GCG to ACG) in codon 148 (exon 2), resulting in an aminoacid change from alanine to threonine. This has previously been reported as a polymorphism. This alteration was also found in the lymphocytes from the same patient. No point mutations or other alterations were found in the sequenced exons from the normal chondrocytes.

Conclusions. Our results indicate that p16 plays a role in the formation of human chondrosarcomas. A definite conclusion can not be drawn until larger materials have been studied and until the whole pathway including CDKN2, CDK4 and the retinoblastoma protein has been investigated.

Sacrofemoral arthrodesis and femoral lengthening osteotomy after internal hemipelvectomy—report of two cases

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Case 1. An 18-year old man had a Ewing sarcoma involving the iliac and sciatic bones with an intra- and extrapelvic soft tissue mass. He had preoperative chemotherapy (VAI-PAI) and radiotherapy (60Gy). Preoperative MRI showed virtually complete regression of the soft tissue mass. The resection (P1 and P2) involved exarticulation of the S-I joint and osteotomy through the superior and inferior branches of the pubic bone. A 10 cm step cut osteotomy of the proximal femur allowed a 5 cm cranial lengthening. The cartilage of the femoral head was removed with a burr and the head was secured to the lateral mass of the sacrum with screws. The operating time was 8 hours and the bleeding 14 L. The postoperative course was uneventful and the patient wore a hip spica for 6 months. One year postoperatively, the patient is fully weight bearing and pain-free.

Case 2. A 56-years old man had a chondrosarcoma of the right pelvis. There was a large intrapelvic soft tissue component arising from the pubic bone and intramedullary tumor was evident up to the SI-joint (Figure 1). The resection (P1, P2, P3) involved osteotomies through the lateral part of the sacrum and the contralateral pubic bone. Similar reconstruction was performed as in Case 1, except that the lengthening was 6 cm, a bone graft was taken from the contralateral iliac crest and placed in the cranial slot of the femoral defect. The operating time was 4 hours and bleeding 10.5 L. Postoperatively there was an undislocated fracture of proximal femur under the plate (Figure 2). 9 months postoperatively, the patient is fully weight-bearing but is treated for poor knee function because of lymphedema.

Figure 1 and 2, se page 43.

High-grade osteosarcoma at the Karolinska Hospital 1991–1996—surgical procedures, reconstructions, and complications

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At our hospital, Interferon was used from 1971–1990 as adjuvant treatment in patients with high-grade osteosarcoma (OS). The overall survival was 50% but the local recurrence rate after limb salvage was 30%. In 1991 we started using neoadjuvant chemotherapy according to the SSG VIII protocol. We present our surgical experiences and complications.

Patients and methods. From 1991–1996 we surgically treated, 28 patients with high-grade, nonmetastatic OS. The chemotherapy was given at the Karolinska or Uppsala Akademiska Hospitals.

Results. A local excison was performed in 19 cases, an amputation in 9. The surgical margin was marginal in 7 and wide in 21 cases. Chemotherapy response was poor in 6 and good in 22 cases. Reconstruction was performed with a massive allograft in 12 cases (6 articular, 5 intercalary, and 1 arthrodesis), vascularized fibula graft in 2, rotational plasty in 2, endoprosthesis in 1, and autograft in 1 case. 11 major complications were encountered: 2 local recurrences (both salvaged and NED), 1 early infection (amputated), 2 late infections (both salvaged), 2 articular allograft failures (both exchanged for endoprostheses), and 5 non-unions or fractures associated with 4 allografts and 1 autograft (3 healed after new osteosyntheses and/or bone transplantation, 1 DOD with pseudarthrosis and 1 persistent pseudarthrosis).

Conclusions. With a high rate of limb salvage procedures we have encountered a high rate of major complications. Nonetheless only 1/19 limbs were lost because of an early infection. Massive allografts seem reliable when used for intercalary reconstruction. A local recurrence rate of 2/19 local excisions seems acceptable but will hopefully improve with the new ISG/SSG I protocol. We will continue our efforts to have an internationally comparable rate of limb salvage procedures.

Osteosarcomas with poor chemotherapy response—better prognosis in patients who developed hematologic toxicity

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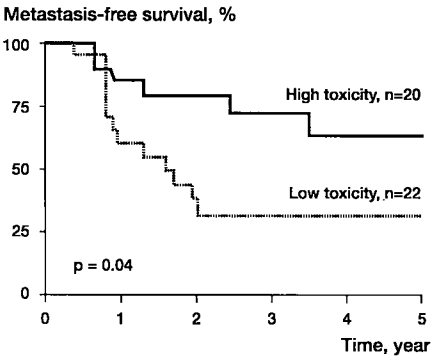
The protocol SSG VIII for the treatment of osteosarcoma was active 1990–1997 and includes 129 patients. The preoperative chemotherapy combines Methotrexate, Cisplatinum and Adriamycin. Histopathological tumor response determines further therapy; continued regimen for good responders and Ifosfamide and VP-16 for poor responders. Tumor response is important for survival with 5-year metastasis-free survival rates of 68% for the good responders and 50% for the poor responders (p=0.01).

We studied the importance of hematological toxicity (WHO criteria)—as a sign of adequate doses—during the preoperative chemotherapy. It was classified as high when toxicity grades I–IV was found in at least 3 of the 6 preoperative chemotherapy phases.

Preoperative hematological toxicity did not influence survival in patients with good histopathological tumor response. However, among 42 poor responders with localized disease at diagnosis, the 5-year metastasis-free survival rates were 63% for the 20 patients who developed hematologic toxicity and 32% in the 22 patients who did not (p=0.04). The corresponding total survival rates were 66% and 47%, respectively, but did not significantly differ. Hematological toxicity did not correlate with dose intensity or dose levels in the preoperative treatment.

Osteosarcoma patients whose tumors show a poor histopathological response to chemotherapy have a worse prognosis. However, our findings indicate that among these patients, those who develop hematological toxicity during the preoperative chemotherapy have better survival.



Prognosis in soft-tissue sarcomas

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We evaluate the outcome and prognostic factors of patients with soft-tissue sarcomas after surgical treatment.

Patients and methods. From January 1979 to July 1993 316 patients with soft-tissue sarcomas in the extremities or truncus, without distant metastasis were treated surgically at the Sarcoma Center in Aarhus. The median age was 56 (1–94) years. 52 patients (16%) had a low grade tumor, 60 (19%) an intermediate and 204 (65%) a high grade tumor. 59 patients (19%) had tumor localized in the upper extremity, 163 (52%) in the lower extremity and 94 patients (30%) presented tumor in the truncus including shoulder and buttock

lesions. 198 tumors (63%) were confined to one anatomical compartment while 118 tumors (37%) spread into two or more compartments. 67 patients (21%) were amputated and 249 patients (79%) had a local resection. 50 patients (16%) received adjuvant radiation therapy and 13 patients (4%) received adjuvant chemotherapy. The minimum follow-up time was 46 months. For the statistical analysis the log-rank test and Cox's proportional hazard models were used.

Results. Local recurrence developed in 59 patients (19%), and the actuarial local relapse rate was 18% at 5 years. Prognostic factors for local control were surgical margin, adjuvant radiation therapy, histological grade and compartmental location of the tumor. 5 and 10-year survival rates were 75% and 67%, respectively. Prognostic factors for survival were age, size of tumor, lower extremity location, histological grade, and compartmental location of the tumor.

Conclusion. Histopathological grade and anatomical extension were the most important factors for local control and survival.

The chromosomal organisation of amplified chromosome 12 sequences in mesenchymal tumors

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Supernumerary ring chromosome and/or giant marker chromosomes, frequently containing amplified material from the long arm of chromosome 12 (12q), characterise a subgroup of mesenchymal tumors of low or borderline malignancy.

We studied the chromosomal organisation of such amplified sequences with fluorescence in situ hybridisation in 8 mesenchymal tumors: 2 osteosarcomas, 1 lipoma and 5 liposarcomas. Amplification of sequences from 12q, predominantly from the region containing the genes HMGIC and MDM2, was confined to rings and/or giant markers in all cases. Alpha satellite sequences from the centromeric region of chromosome 12 was detected in rings and markers in 5 cases. Telomeric and subtelomeric sequences were present in ring chromosomes in 1 case. Both osteosarcomas, but none of the lipogenic tumors, also contained amplified material from the short arm of chromosome 12, indicating a distinct genetic difference between these tumor types.

Single-copy probes demonstrated considerable inter- and intracellular variation in the arrangement of sequences in ring and marker chromosomes. This could be partly explained by continuous recombination through breakage-fusion-bridge cycles.

Clinical relevance of type of SYT/SSX fusion gene in synovial sarcoma

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Synovial sarcomas carries the translocation t(X;18)(p11;q11). This translocation results in the fusion of the SYT gene to one of two SSX genes (eg. SSX1 and SSX2). This fusion gene can be detected by reversed transcription polymerase chain reaction (RT-PCR. This study aims to investigate whether the type of translocation (SYT/SSX1 or SYT/SSX2) may be correlated to the clinical behaviour of synovial sarcoma. For this purpose we have analysed 45 fresh frozen biopsies of synovial sarcoma. All these cases are included in the SSG registry. Results obtained will be presented as a poster.

Fine needle aspiration cytology of spindle cell lipoma

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Spindle cell lipoma (SCL) is a slowly-growing, benign fatty tumor usually arising in adult men. The tumor is subcutaneous and most frequently located in the upper back and neck. Fine needle aspiration cytology (FNAC) from SCL is insufficiently defined and shares some features with other spindle cell or myxoid lesions, benign as well as malignant.

Study design. We reviewed FNA findings of 7 cases of SCL and correlated with clinical data and subsequent histology. In 3 cases chromosome analysis was also performed on the surgical specimens.

Results. Most of the smears showed a distinct cytologic pattern but variable cellularity. 3 aspirates were reported as SCL, 3 as "benign soft-tissue tumor" while 1 as "benign process in soft-tissue". Predominantly spindle-cells areas were observed in 2 excised tumors and a scanty spindle-cell component in 1. Chromosome analysis in 3 cases showed the typical aberrations: 16q and 13q deletion.

Conclusion. FNA diagnosis of SCL is possible when the clinical data are typical and the aspirate contains a mixture of benign adipose tissue and fascicles of spindle cells in a collagenous/myxoid background. Chromosome analysis is of diagnostic help since the histologic picture occasionally is not sufficiently specific.

Establishment of clear cell sarcoma xenograft model in nude mice

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Clear cell sarcoma is a soft tissue tumor possessing melanocytic features and is intimately associated with tendons and aponeuroses. The purpose of our study was to establish a human clear cell sarcoma xenograft model in nude mice using subcutaneous transplantation of intact tumor tissue.

Methods. Tumor growth, structure and cell proliferation were studied during 5 serial passages. Growth was expressed as volume doubling time (VDT). Structure was assessed by analysing tumor ploidy, cytogenetics, histopathological appearance, expression of melanoma antigen (HMB45) and S-100 protein. Cell proliferation was analysed by in vivo labelling with the thymidine analogue iododeoxyuridine using immunohistochemistry and by using immunohistochemical staining against Ki67 proliferation antigen.

Results. Histopathological characteristics of the donor patient's tumor, as well as expression of melanoma antigen and S-100 protein, were retained during serial transplantation. Mean volume doubling time was 9.2 days (SD 2.7) and 8.9 days (SD 2.3) in the third and fourth passage respectively. Both growth and cell kinetic parameters showed low variations between passages and between xenografts in the same passage.

Conclusion. This novel clear cell sarcoma tumor model is suitable for further studies on tumor biology and evaluation of new treatment modalities

Intratumoral DNA ploidy heterogeneity in soft tissue sarcoma

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DNA-ploidy may give prognostic information in soft tissue sarcoma (STS). However, few have studied intratumoral DNA-ploidy variation.

Patients and methods. We studied DNA-ploidy with flow cytometric analysis (FCM) in 79 STS (67 primary tumors and 12 recurrencies or metastases). Two different samples were analysed in 53 tumors, 3 samples in 14, and 4 samples in 12 tumors. Intratumoral heterogeneity was defined as the presence of DNA histograms with different ploidy in different samples of the same tumors. Tumors with heterogenous FCM ploidy status or with all FCM samples diploid, were also analysed by image cytometry (ICM).

Results. In 48 tumors all samples were non-diploid. A heterogenous FCM ploidy status was found in 10 tumors. Further analysis with image cytometry (ICM) of these 10 tumors demonstrated non-diploidy in all samples of 5 tumors; the other presented heterogeneity also on ICM (1Auer II/I, 1 AuerI/IV, and 3 Auer III/IV). In 21 tumors all FCM samples were diploid, but ICM demonstrated heterogeneity in 5 tumors (2 Auer I/II, 1 Auer I/III, and 2 Auer I/IV).

Considering the combined FCM/ICM evaluation, heterogenous DNA-ploidy status was present in 10 tumors, in 5 of 53 tumors where 2 samples were analysed, in 2 of 14 with 3 samples, and in 3 of 12 with 4 samples.

Conclusion. variation in DNA ploidy status can not safely be based on only FCM analysis which may miss some non-diploid clones. Additional ICM analysis showed that only 10 of 79 tumors were ploidy heterogenous.

Comparison of DNA ploidy measurement performed by flow and image cytometry in soft tissue sarcoma

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DNA ploidy measurements can be performed with flow cytometry (FCM) or image cytometry (ICM); both methods provide independent prognostic information in some malignant tumors.

Patients and methods. In 85 primary soft tissue sarcoma the two methods were tested on the same tumor specimen and the finding related to the prognosis after a minimum follow-up of 2 years for the survivors.

Results. Identical ploidy status (diploid vs. non-diploid) was obtained in 70 tumors (concordance rate 82%). Of the 18 FCM-diploid tumors, 12 were diploid also on ICM (one population), and 6 were non-diploid (5 with 2 populations and 1 with 3 populations). Of the 67 FCM-non-diploid tumors, 9 were ICM-diploid.

3 of 12 patients with diploid tumors by both methods, 2 of 6 with FCM-diploid but ICM-non-diploid, 1 of 9 with FCM-non-diploid but ICM-diploid, and 28 of 58 (0.5) with non-diploid tumor by both methods died from tumor.

Conclusion. By ICM it is possible to identify non-diploid populations in one third of FCM-diploid histograms. The clinical value of this finding remains unclear.

Fine needle aspiration (FNA) of soft tissue leiomysarcoma

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We investigated whether leiomyosarcoma had a reproducible, characteristic pattern in FNA. 70 aspirates of extremity and trunk leiomyosarcoma were reexamined. Fine needle aspirates from primary, recurrent and metastatic tumors were included.

The yield was predominantly high to moderate. The cellular pattern was that of a spindle cell or pleomorphic sarcoma or a mixed pattern. Cell rich cohesive, sometimes fascicular micro biopsies were typical in the spindle cell pattern.

Cells with blunt ended, truncated nuclei with often prominent nucleoli and blue grey (MGG) or eosinophilic (HE) uni-or bipolar cytoplasm were always part of the smears. In the pleomorphic and mixed patterns cells with variable sizes and shapes were predominant. Bi-or multinucleated cells with abundant cytoplasm were always present as spindly cells with blunt ended nuclei

Common for all patterns were numerous stripped, sometimes deformed nuclei.

The most important diagnostic pitfalls were ancient neurilemoma and leiomyoma of the deep soft tissue and pleomorphic sarcoma of non myogenic origin, metastatic spindle cell carcinoma and sarcomatous melanoma.

Conclusion. Leiomyosarcoma of the soft tissue has a variable but mostly recognizable pattern in FNA. Electron microscopic and/or immunocytochemical examinations of the aspirate are valuable adjuncts to a reliable diagnosis.

Chondroid lipoma—ultrastructural aspects on a new entity—a case report

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Chondroid lipoma was recently (1993) described by Meis and Enzinger. This benign lesion can be mistaken for a myxoid liposarcoma, extraskeletal myxoid chondrosarcoma or hibernoma. We here report the ultrastructural findings of this rare tumor.

Clinical history. A 19-year-old man had a deep-seated tumor of the left calf, 5 cm in greatest dimension. Fine needle aspiration (FNA) was followed by surgery. At gross examination the tumor was intramuscular, encapsulated, firm and yellow. Both FNA cytology and histology showed a lipomatous tumor with hibernoma-like features, lipoblasts and chondroid matrix. Cytogenetic analysis revealed at (11;16) translocation.

Electron microscopy. At low magnification mature adipocytes were intermingled with small cells arranged in strands and groups or as isolated elements in a hyaline matrix. The spectrum of lipogenic differentiation ranged from primitive cells to lipoblast-like cells and mature adipocytes.Some of the undifferentiated tumor cells contained few small lipid droplets and abundant organelles while others were multivacuolated and contained few organelles. The nuclei were irregularly shaped and deeply clefted, sometimes with pseudoinclusions. The cell membrane had pinocytotic vesicles and incomplete external lamina. The lipoblast-like cells had numerous cytoplasmic lipid droplets and scalloped nuclei. The adipocytes had one or two large lipid droplets and peripherally compressed crescent-shaped nuclei. Knob-like protrusions of the cell membrane were noted. The extracellular matrix was composed of thin collagen fibers and proteoglycan-like particles in a flucculent background.

Conclusion. Electron microscopy of chondroid lipoma helps to diagnose and to understand the histogenesis of this rare benign lesion

The role of amputation in advanced soft tissue sarcoma

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Local control is very important in sarcoma surgery, regardless of its questionable impact on survival. A negative surgical margin is mandatory to avoid local recurrence and thus in many cases amputation is justified. Local control appears to be more frequently achieved after amputation than limb-salvage surgery. Among the Scandinavian Sarcoma Group Centres there is a clear positive correlation between amputation rate and local control. The ultimate amputation rate in "limb-salvage centres" utilising multimodality treatment, equals the amputation rate in centres were surgery was the mainstay in treatment. Complications are much more frequent and severe after limb-salvage surgery, than after amputation. Function and quality of life do not differ significantly between amputees and limb-salvage patients.

Conclusion. Adequate surgical procedures preceded by well planned biopsies or cytologic aspirations will locally control 90 % or more of soft tissue sarcomas of the extremities. Approximately 15 % of patients need an amputation. These candidates for amputation are not better off, some probably worse off, with limb-sparing surgery and the adjuvant treatment that is available today.

Is preoperative radiotherapy in soft tissue sarcoma worthwhile?—the results of a pilot study

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It has been stated that radiation therapy of soft tissue sarcomas will eventually "sterilize" the tumor surface, thereby allowing a more conservative approach and yet not jeopardize a low local recurrence rate. To evaluate this and other aspects of preoperative radiotherapy we undertook a pilot study.

Patients and methods. 11 consecutive patients (8 M/3 F) with an average of 57 (26–80) years with confirmed cytologic diagnosis of malignant fibrous histiocytoma (6), unclassified high-grade sarcoma (2) and myxoid liposarcoma (3) received 46 Gy (23x2.0 Gy) preoperatively. The median tumor

size on MR was 11 (5–21) cm. Surgery was scheduled 2–3 weeks after completed radiotherapy.

Results. The average delay from diagnosis until start of radiotherapy was 24 days, and surgery was performed at an average of 77 (56–107) days after diagnosis. 9 patients had local excisions (6 wide/3 marginal), 1 had a wide amputation, and 1 was inoperable at the time of planned surgery. Radiotherapy was clearly effective in the 3 patients with myxoid liposarcomas; all became largely acellular, partly necrotic and showed maturation of the lipomatous tumor component. In the other 8 cases substantial amounts of viable tumor cells could be identified, also on the tumor surface, and no fibrous encapsulation was noted. In only one of these cases a significant reduction in the size of the tumor could be attributed to radiotherapy. Wound rupture/necrosis occurred in 4 patients of which 3 required surgical management. 1 more patient was reoperated because of symptomatic seroma. Altogether, only 3 out of 9 patients with local surgery had a primary complication free wound healing.

Conclusions. Preoperative radiotherapy is a very valuable adjuvant in the local treatment of myxoid liposarcomas. However, our experience of radiotherapy in other types of deep-seated soft tissue sarcomas is rather dismal. The histologic findings indicated that narrower surgical margins could not be applied. The possible consequences for the patient of more than 3 weeks of delay in any kind of treatment and 2+ months of prolonged hosting of the tumor were of great concern. The high complication rate was discouraging. Our findings are in discordance with most published series and have prompted us to close the present study in favor of a planned alternative protocol.

Figure 1

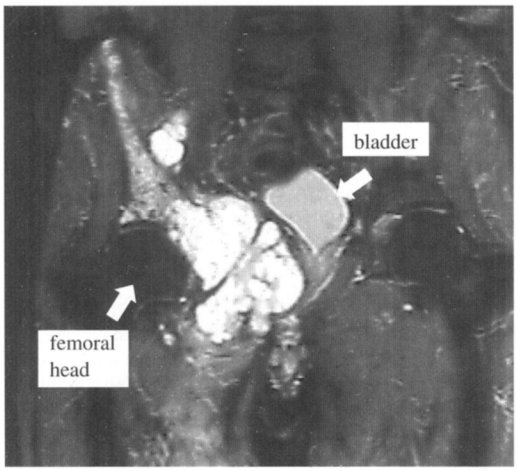

Figure 2