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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.

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Diagnostic work-up of soft tissue sarcomas: compliance with the guidelines

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Background: National guidelines for the diagnosis and treatment of patients with soft tisssue tumours aim to optimize treatment and to avoid unplanned "Oops"-resections of soft tissue sarcomas (STS) In the present study adherence to national guidelines (2003) was evaluated.
Material and Methods: A population-based cohort of patients with primary STS of the extremities and truncal wall was analysed. Patients were registered and treated in the area of the Comprehensive Cancer Centre Middle Netherlands between January 1991 to January 2008. We evaluated the proportion of patients that had preoperative imaging of the tumour, preoperative histological biopsy and radiological examination for pulmonary metastases. A possible effect of the national guideline was studied by comparing the results for the cohorts treated before and after 2003.
Results: The case records of 326 patients were evaluated. There were 192 males and 134 females with a mean age of 54 years. The STS were localized on the legs in 160 patients (49.1%), the arms in 62(19%) and truncal wall in 104 Patients (31.9%). Preoperative work-up contained an MRI in 58.3% of the patients, a histological biopsy (incisional or core needle) in 39%, and chest X-ray or CT in 62.2%. Patients with a STS of the lower extremity more often had preoperative MRI-scans than patients with STS located in the upper extremity or the truncal wall ($p = 0.048$). In the recent cohort it seems that better imaging of the primary tumour was done, while the proportion of patients that had preoperative histological biopsies and chest staging remained the same.
Conclusions: Guideline compliance in patients with STS in the extremities or truncal wall appears poor. In recent years there seems to be a trend towards better imaging, but not biopsying or staging of the STS.

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The role of postoperative radiotherapy in nonmetastatic soft tissue sarcomas of the extremities: a monocenter results

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Purpose: To assess the results of postoperative radiotherapy in patients with nonmetastatic soft tissue sarcomas of the extremities and the prognostic factors that affect the treatment results, respectively.
Methods and Materials: Between the years 1980 and 2005, 103 patients with sofy tissue sarcomas of the extremity treated in our department.53 (51.5%) were male, 50 (48.5%) were female. Median age was 43 years (range 15−92 years). The tumor size was between 1−22 cm (median 8 cm). Nine patient stage IA, 41 were stage IB, 10 were stage IIA, 22 were stage IIB, 9 were stage IIIA, 12 were stage IIIB. The most frequent histological types were; malignant fibrous histiocytoma (27.9%), liposarcoma (23.1%) and synovial sarcoma (13.5%). Twenty-five patients were operated for reccurent tumor before they were refered to our clinic. Anteropsterior and posteroanterior parallel-opposed ports were usually used and a booster dose was given after 45−46 Gy. The median total tumor dose was 62 Gy(median 46−70 Gy).49 patients had close or positive surgical margin. Adjuvant chemotherapy was added to the patients with high grade tumors. Chemotherapy was given in 39.4% of the patients. Chemotherapy scheme consisted of doxorubincine 75 mg/m^2, ifosfomide with mesna 2 gr/m^2, used in different combinations. Treatment results were analyzed by Kaplan Meier metod and univariate and multivariate analysis was performed.
Results: Median follow up time was 60 months (range 3−349 months).24 patients (23.3%) locally recurred and 30 Patients (29.1%) had distant metastases. Lung and bone metastasis were the most common site of metastasis. The 5 year local control, disease free and overal survival rates were 76%, 58% and 71%, respectively. Tumor size >5 cm had a worse prognosis than smaller tumors at overall survival in univariate analysis ($p = 0.05$). Patients treated with dose >60 Gy($p = 0.04$) and lower extremity located tumors had significantly better local control than the others ($p = 0.04$). In multivariate analysis both radiotherapy dose and ($p = 0.04$), tumor size >5 cm ($p = 0.03$) and location of the tumor($p = 0.04$) were found to be significant prognostic factors. Hyperpigmentation and desquamation was the most common frequently seen early side effect. 45 patientshad various degrees of fibrozis, 15 patients had chronic oedema, 7 patients had delayed wound complication, 3 patient had lympangitis and 1 patient had bone fracture as late morbidity.
Conclusion: Postoperative radiotherapy has an important role on local control of extremity soft tissue sarcomas. Tumor location, tumor size and radiotherapy dose seems to be the most important prognostic factors affacting the treatment results in our series.

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Retroperitoneal sarcoma: retrospective analysis of a large single institution series

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Background: Prognosis of retroperitoneal sarcoma (RPS) is poor, especially if evaluated on the long run. The majority of patients die of loco-regional disease. The mainstay of treatment for primary and recurrent RPS is surgery, but both quality and efficacy of the surgical resection decrease after multiple recurrences. We analyzed a large single institution series of RPS with the aim to provide information on the natural history of the disease and to identify prognostic factors of outcome.
Methods: since 1998 to 2008, 149 patients referred to our Institution underwent surgery for RPS (77 primary tumors, 72 recurrent). Potential prognostic factors including histology, tumor grading, time to last recurrence and multifocality were retrospectively tested by univariable and multivariable analysis. Primary end-points were local disease free survival (LDFS) and disease-specific survival (DSS) from the first recurrence onward.
Results: Median age of the study population was 55 years (range 20−83); 81 were male. Median FU was 33 months (range 6−122). 5-year LDFS and DSS for the whole population were 27.6% and 86%, respectively. Nine-teen patients (13%) developed distant metastases (63% pulmonary; 68% extrapulmonary). Among these, only one was affected by liposarcoma. Twenty-six primary tumors (33.8%) required multivisceral

associated resection (32% leiomyosarcoma; 14% liposarcoma; 14% other histology). LDFS and DSS became increasingly shorter along with the number of recurrences. Histology and tumor grading have been identified as independent prognostic factors for LDFS. Sex and grading predicted DSS.
Conclusions: In our series, leiomyosarcoma needed a higher rate of multivisceral resections than liposarcoma, probably due to their infiltrative growth pattern, nevertheless, liposarcoma had a worse local control (5-year LDFS 18% versus 56%). Long term survival was similar (5-year DSS 87.6% versus 80.5%), due to the lower rate of distant metastases in the liposarcoma subgroup. The poor local control of liposarcoma, in front of an apparent gross pushing growth pattern, arises the question if a more aggressive surgical policy should be adopted. Recurrent and multifocal tumors need a multimodality approach, since the low chance of radical surgery.

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"Oops procedures" of Soft Tissue Sarcomas (STS) of extremity and superficial trunk

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Background: Compared to the very common soft tissue masses of the extremities and trunk, soft tissue sarcomas (STS) are rare. Despite national guidelines advocating investigational work-up of soft tissue tumours larger than 5 cm or localised under the fascia, STS are sometimes resected unplanned. The aim of the present study is to describe the frequency of these "Oops procedures", and to determine the proportion that was resected ignoring the guidelines.
Material and Methods: A population-based study was conducted in the area of the Comprehensive Cancer Centre Middle Netherlands. Patients treated between 1992 and 2006 for a STS of the extremities or trunk were identified and case records were retrieved from the five hospitals within the area. We analysed the proportion of patients who had an unplanned marginal resection of a sarcoma, i.e. without preceding MRI or pathology examination. In addition, we analysed which Oops resections could have been prevented if surgeons had acted in accordance with the guidelines, and which cases should be considered 'unpreventable' since they were superficially localised and smaller than 5 cm.
Results: A total number of 326 patients were treated for a primary STS in the extremities or trunk There were 152 male patients (58.9%), and the mean age at presentation was 53.6 years. The median size of the STS was 8.3 cm, and 53% of the tumours was superficially localised.
Twenty-four percent of the patients underwent un unplanned excision as a first operative procedure. Patients who underwent "Oops" procedure had tumours that were smaller (22% <5 cm vs 81% <5 cm; $P < 0.001$), tumours that were more often superficially localised (74.3% vs 44.5%, $P < 0.001$). Furthermore, localisation of the STS influenced the chance of an unplanned resection (46.8% of the lower extremity, 24.1% of the upper extremity, 29.1% for tumours of the trunk). Of the patients that underwent an Oops procedure approximately 30% had tumours that were larger than 5 cm and/or deeply localised. Thus 7.5% of all patients underwent an unplanned resection that could have been prevented when guidelines would have been adhered to.
Conclusion: One quarter of all patients that have STS in the extremities or trunk underwent an unplanned resection. In 7.5% the unplanned resection was the result of non compliance to national guidelines. By defining the quantity of these "Oops procedures", we hope to provide more insight in the current situation of these sarcomas and hereby improve the treatment and outcomes for the patient.

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The role of chemotherapy in aggressive fibromatosis

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Background: Despite the absence of metastatic potential, aggressive fibromatosis [AF] can be life threatening due to its locally invasive behaviour. The mainstay of treatment is surgical resection with or without radiotherapy. Patients with inoperable disease may be managed with systemic therapy. Chemotherapy is usually administered following failure of hormonal therapy and/or NSAIDS or in the presence of rapidly progressing disease. A number of studies have reported a variety of effective regimens, predominately involving combination therapy with two cytotoxic agents.
Materials and Methods: We conducted a retrospective search of our prospectively maintained database to identify AF patients treated with chemotherapy between 1987 and 2008. The majority of patients were referred to our institution following diagnosis, and in certain instances initial management, at other non-specialist centers.
Results: Thirty six patients with progressive or recurrent AF received one or more lines of chemotherapy. The female: male ratio was 28:8 and median age at presentation was 26 years (range 3−54). Most patients had surgery (30/36 = 83%) and/or radiotherapy (20/36 = 55%). Twenty eight patients (77%) received hormonal treatment usually prior to chemotherapy. The most frequently employed chemotherapy regimens were methotrexate [MTX]/vinblastine (17) and liposomal doxorubicin [LD] (11). Other combinations/agents included MTX/other vinca alkaloid (3), doxorubicin/DTIC (5), vincristine/actinomycin D (2), ifosfamide (2) and other (5). In the MTX/vinblastine group response data were available in 70% of cases. Treatment duration was 3 weeks to 1 year; disease stabilisation was seen in 7/12 (58%) cases; disease progression in 3/12 (25%). Symptomatic benefit was reported in approximately 50% of patients. Peripheral neuropathy and vomiting were the most severe toxicities. Pegylated LD chemotherapy was given at 40−50 mg/m^2 q 4 weeks, for up to 6 cycles. Objective response (PR) according to RECIST was achieved in 4 patients (36%) but notably in some cases not until 6−12 months after completion of chemotherapy. In the remaining 7 cases the disease was stable with no progression during treatment. Symptomatic benefit, especially pain relief, was reported in all cases. Main toxicities involved skin and oral mucosa.
Conclusion: Chemotherapy is a valuable tool in the management of AF. MTX/vinblastine remains a useful combination but LD is emerging as a well tolerated and effective single agent in unresectable AF.

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Clinical outcomes in patients with a dermatofibrosarcoma protuberans, the effect of microscopic clear resection margins on survival

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Background: Dermatofibrosarcoma protuberans (DFSP) is a rare cutaneous sarcoma. The local agressiveness of DFSPs commonly necessitates extensive resections to obtain tumourfree resection margins. We evaluated outcome of patients with DFSP in relation to resection margin status and postoperative radiotherapy.
Material and Methods: A population based cohort of patients with primary DFSPs treated in the middle Netherlands and registered between 1991 and 2008 by the Comprehensive Cancer Centre was analysed. All patients underwent surgery. Radiotherapy was not uniformly applied. Case records were studied retrospectively, median follow-up was 56 months.
Results: Forty patients underwent surgery for DFSP with a median age of 43 years, gender was evenly distributed. Eighty percent of the tumours was localised on the trunk or upper extremities. Microscopic tumour free resection margins were obtained in 36 patients, multiple resections were needed in seven of them (19%). Seventeen patients had postoperative radiotherapy (following a radical resection). At the end of follow-up, one patient had died of pulmonary metastases, 4 patients had developed a local recurrence. Two of these recurrences developed after an initial irradical resection. The overall five-year cumulative local recurrence rate was 14%. Given a microscopic complete resection, no effect on local recurrence was seen of postoperative radiotherapy.
Conclusions: In a population-based series of patients with locoregional DFSP, obtaining tumour-free resection necessitated repetitive surgery in a substantial proportion of patients. Following resection with microscopic clear margins, local recurrence rates were low, irrespective of postoperative radiotherapy. In a selection of patients with DFSP, postoperative radiotherapy might be avoided.

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Pre-operative intensity modulated radiation therapy (IMRT) in retroperitoneal sarcoma treatment

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Purpose: Retroperitoneal sarcoma (RPS) recurrences are frequent, due to difficulties to obtain complete surgical resection and proximity of organs at risk limiting radiation doses. The purpose of this study is to assess the outcome of patients with RPS, treated with pre-operative IMRT.