

significance for response ( $p = 0.013$ ). Particular metastatic sites were not influential for response, but predominant retroperitoneal metastases in STS patients were associated with longer time to progression ( $p = 0.013$ ).

**Conclusion:** response rate (RR) and median time to progression are in the limits reported for advanced soft tissue sarcomas (STS), as well as high histological grade (G3) as prognostic factor for response. Peculiar result is that retroperitoneum as predominant metastatic site displays significance for time to progression.

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## PUBLICATION

### Short-term evaluation of gait in patients after limb-sparing surgery (LSS)

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**Purpose:** At the moment it is not clear how LSS, when applied to lower limbs, does lead to optimal functional results i.e. optimal walking capacity in everyday situations. For walking in an automated fashion a complete re-organisation of the control mechanism is needed.

**Methods:** We studied 11 patients who had a follow-up starting 5 months till 15 months after operation. We measured normal walking, and walking under constraints on a treadmill. The constraint was visual and cognitive. The influence of these constraints on their walking could be derived from basic gait parameters i.e. stride duration.

**Results:** During the follow-up the patients showed an increase in walking speed, a decrease in step cycle duration, a decrease of the influence of walking constraints on stride parameters, a distinct improvement in left-right asymmetry overtime and an improvement of motor skills.

**Conclusion:** A clear functional improvement of gait over a period of 15 months. Which means that in a rather small period they are able to re-organize the massive loss of proprioception due to the surgery. However, during gait with different type of constraint, these patients showed some remaining deficits.

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## PUBLICATION

### Histologic types of post radiation sarcomas

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Post radiation sarcomas are a rare entity and large series are rarely reported. We retrospectively reviewed the cases treated in the French Cancer Centers. All cases were reviewed by a panel of pathologists.

From 1975 to 1995 125 cases were referred for treatment and in 80 cases the diagnosis of sarcomas was confirmed. 56 developed in soft tissues and 24 in bone. Histologically there were: 24 Malignant Fibrous Histocytomas, 5 osteosarcomas, 6 fibrosarcomas, 7 Angiosarcomas, 32 miscellaneous in Soft tissue; 14 Osteosarcomas, 5 Malignant Fibrous Histocytomas, 5 miscellaneous in bone. The tumors were graded with the FNCLCC grading. This was possible in 56 cases and we looked at the survival according to the grade. It was statistically significant.

	Soft tissue	Bone	Total	survival 2 yrs	survival 5 yrs
Grade 1	6	0	6	33%	17%
Grade 2	15	2	17	76%*	62%*
Grade 3	26	5	31	41%*	19%*

\*  $p < 0.01$

**Conclusion:** The majority of postradiation sarcomas was of Malignant histioblastoma type and osteosarcoma type. Most was of high grade. Survival is affected by the grade

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## PUBLICATION

### Can multimodal therapy improve the situation of retroperitoneal sarcoma? A prospective analysis

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**Objektive:** Retroperitoneal sarcoma are rare malignant soft tissue tumors occurring in only 0.1–0.2% of all malignancies: We reviewed the occasion,

clinical course, therapeutic and pathologic characteristics of patients (pts) underwending treatment in our hospital in the last years.

**Patient characteristics:** We evaluated 30 pts in our prospective analysis. The median age at diagnosis was 59.1 (8–74) yrs; sex 17/13-m/f. The most common histologic types were liposarcoma (14) and leiomyosarcoma (10). 28 pts received surgery as first line treatment, 20 an en bloc resection, 7 a wide resection and 1 a quadrantenresection, two pts were inoperabel. 14 pts underwent one or more adjacent organ resection to achieve a total excision (kidney 6x, adrenal gland 2x, uterus/adnexe 5x, spleen 1x, colon 3x, small intestine 2x). V. cava was involved in 3 cases.

**Results:** Postoperative 8 pts recieved adjuvant radiotherapy (aRT), in 6 cases adjuvant chemotherapy (aCT) was administered. 14 pts only underwent surgery. A local relapse appeared in 14 cases, other 3 had a distant failure. The rezidivrate after aRT was 50% ( $n = 4$ ), after aCT 66% ( $n = 4$ ) and after surgery alone 42.8% ( $n = 6$ ). Metastasis occurred in two pts. after aRT and in one without adjuvant treatment. The median time to rezidiv was 22 months, to metastasis 11.2 months. In 64% the rezidiv occurred in the first 24 months. According the Kaplan-Meier method the probability for 5-year survival is 82% with aRT, 27% with aCT and 46% receiving surgery alone. At this time 9 pts-died because of their disease.

**Conclusions:** The combined treatment surgery with adjuvant radiation or chemotherapie can't improve the rezidivrate or the disease-free-survival. But the application of aRT seems to be sufficient for a better survival in our pts.. Randomised studies are indicated to evaluate combined modalities improving the local treatment and the long-term-survival and preventing systemic relapse.

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## PUBLICATION

### Is there a place for taxoids in patients with advanced sarcomas?

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**Purpose:** following data of Lyden about the high efficacy of taxol in mice with either alveolar or embryonal rhabdomyosarcoma (RMS) (Med. Ped. Onc. Vol. 29, 5, 1997, 067) we decided to test the efficacy of taxoids in advanced sarcomas.

**Methods:** in 3 cases of advanced sarcomas, we tested a salvage chemotherapy (CT) with taxoids. We treated a 21 y. old girl with metastatic RMS with a second peritoneal relapse with taxol, 4 cycles of 435 mg/m<sup>2</sup> per cycle (145 mg/m<sup>2</sup> D1, D5 and D9 docetaxel) every 3 wk. A second patient (p.), 27 y. old, with an huge pulmonary metastatic osteosarcoma (OS) was treated by taxol with the same scheme. A third p., 20 y. old, with bone metastatic OS was treated by Docetaxel 100 mg/m<sup>2</sup> every 3 wk as a fourth line therapy.

**Results:** the 3<sup>rd</sup> p. had an objective partial response (duration of response: 6 months in case 1 and 2, 4 in case 3). In the first case, side effects of taxol were mild: anorexia, headaches and gastric pain, erythema and cutaneous hyperesthesia at the end of each course despite of the high dose of taxol. In the second case, asthenia, exfoliation grade II, cumbersome nails changes were deeply marked. Side effects of docetaxel were limited to diarrhea and grade III neutropenia.

**Conclusion:** Taxoids had a definite effect on highly pretreated sarcomas. Further studies with its use as second line therapy, could help to determine better its role in sarcomas. 8

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## PUBLICATION

### Extremity osteosarcomas: Intraarterial chemotherapy

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**Purpose:** To evaluate the efficacy and toxicity of neoadjuvant chemotherapy (intra-arterial) in extremity osteosarcomas.

**Methods:** Since 12/90, 12 patients (pts) have received neoadjuvant chemotherapy: intra-arterial cisplatin (150 mg/m<sup>2</sup>) and CVP adriamycin (90 mg/m<sup>2</sup>). The median age was 18.5 years (15–35 y); 7 females and 5 males; sites: femur-8 (distal-7, proximal-1), tibia- 4; tumour size >5 cm–10 (83.3%).

**Results:** Total of 42 cycles, only 36 cycles were delivered by intraarterial infusion (median-3.5 range 1–4) due to local complication in 2 pts.

Limb-sparing surgery was performed in all pts; 2 achieved ≥90% necrosis, 8 < 90%, 2 were not evaluated. One pt had radiotherapy after. Eleven pts received adjuvant chemotherapy, in 9 pts- cyclophosphamide, bleomycin, actinomycin D, etoposide, cisplatin, adriamycin and in 2 pts- adriamycin. Recurrent disease was found in 4 pts: local-2, distant-1, local + distant-1

Toxicity (WHO)	G0	G1	G2	G3	G4
Anaemia	3	1	4	3	1
Granulocytes	3	1	3	4	1
Platelets	4		1	4	3
Hearing	9	1	1		1
Renal	8	2	2		

(DFS: 2–17 m). Five amputations were required, due to local recurrence-3 and prosthesis problems-2. At a median follow-up- 25 months (11–99 m), 9 pts- alive (disease free) and 3 pts- dead.

**Conclusion:** Intra-arterial chemotherapy is an effective and tolerable regimen that produces acceptable rate of limb sparing surgery in extremity osteosarcoma.

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PUBLICATION

### Kaposi's sarcoma: Chemotherapy. Retrospective analysis

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The cases of 43 patients with Kaposi's sarcoma (KS), assisted at our clinic between 1994 and 1998, were retrospectively reviewed. The demographic characteristics were as follow: 38 patients were seropositive for HIV 1 and 5 negative; 39 patients were males. Median age at diagnosis was 36.3 years for HIV+ patients and 65.2 for seronegatives. Homosexual contact was reported in 41% of HIV+ patients and in none of the HIV-. At the time of diagnosis, 87% of the patients presented with more than 10 lesions, 54% were T1, 78% were I1 and 66% were S1. 56% of HIV+ patients were CDC C3. Chemotherapy was administered to 33 patients, with either Bleomycin plus vincristine (BV), liposomal daunorubicine (dauno) or liposomal doxorubicine (doxo), in standard dosage regimens. The following results were observed: 16 patients with BV (total of 145 cycles), with 7 partial responses (PR), 4 stable disease (SD), 4 progressing diseases (PD), and 1 not evaluable (NE); 9 patients with dauno (total of 64 cycles), with 1 complete response (CR), 3 SD and 5 PD; 16 patients with doxo (total of 114 cycles), 1 CR, 10 PR, 2 SD and 3 NE. Grade III/IV toxicity was observed with doxo (4 cutaneous) and dauno (neutropenia in 8 cycles).

**Conclusions:** patients in this retrospective study, were predominantly male, 41% had confirmed homosexual contact. The best results were observed with doxo monotherapy, followed by BV. Good response to doxo in HIV- patients was also observed. Doxo also showed the more severe toxicity, with 4 cases of palmoplantar erythema, and desquamation, which led to suspension of treatment in 3 patients

**Conclusions:** Robust methodology for synthesising evidence is crucial. Systematic reviews improve our understanding of effectiveness and help plan new trials. The Cochrane Cancer Network (supported by BIOMED 2) is to produce a "cancer library". This will include the most comprehensive register of controlled cancer trials to date and databases of Cochrane and other systematic reviews. It will be available on the Internet from May 2000. New reviewers are needed by Cochrane Cancer Groups to help in the huge effort to produce a coherent foundation of systematic review evidence which can be used to develop better trials and help make better decisions for the individual patient and health care services.

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ORAL

### The development of clinical guidelines for oncology in France

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**Purpose:** Since 1993 the French Federation of comprehensive cancer centers (FNCLCC) has been developing clinical practice guidelines (CPG) for oncology known as the Standards, Options and Recommendations or SOR. The SOR project was initiated by health professionals themselves. The primary objective of the SOR project is to develop clinical practice guidelines to improve the quality of health care and patients outcomes in oncology.

**Methods:** The guideline development process involves multi-disciplinary groups. A systematic literature review is performed to developed evidence-based recommendations in a process involving feedback from specialists in cancer care delivery, are developed for all aspects of patient management from diagnosis to supportive care. The initial guidelines are being updated. Dissemination occurs at national and local levels, and the SORs are implemented at a local level by the cancers centers and on the regional levels by cancer networks.

**Results:** A total of 45 guidelines has been already published using both paper and electronic supports. A recent study on dissemination and implementation in the 20 cancers centers showed that 98% used the guidelines even if it was not always for patient care.

**Conclusion:** The SOR development team will now need to address research on understanding determinants of the guideline development process, the definition of quality criteria, the integration of cost issues, the updating process, the legal implications of guidelines and the evaluation of their impact on clinical practice.

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ORAL

### Risk of late stage breast cancer following a childbirth

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**Background:** A pregnancy may lead to hormon-induced growth of breast tumors. We investigated whether women in the first years following childbirth had a higher incidence of breast cancer and in particular a higher incidence of late stage tumors compared to other women.

**Methods:** The study was based on a population based cohort of 1.5 million Danish women born 1935-1978 with individual information on births. Between 1978 and 1994, 10,790 incident cases of breast cancer were identified in a nationwide cancer registry which includes detailed information on tumor characteristics at diagnosis.

**Results:** Overall uniparous and biparous mothers experienced a transient increased risk compared to women with one birth less. The risk of being diagnosed with a tumor with a diameter larger than 5 cm was on average 53% higher the first 10 years after birth compared to later. The pattern was the same irrespective of parity. The risk of tumors less than 2 cm was not significantly associated with time since latest birth. Similar patterns were found when we instead of tumor size used nodal status or histological grading as stage dividing criteria. The increased risk could not be attributed to delayed cancer diagnosis.

**Conclusion:** After a childbirth mothers experience a transient increased risk of breast cancer and in particular a relatively high risk of late stage disease. This finding suggests that pregnancy related factors transiently induce a high growth rate in cells that are already malignant and induce new tumor growth.

## Epidemiology and communication

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ORAL

### Organising & using evidence from randomised controlled trials in cancer: Co-ordination and dissemination

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**Purpose:** We have, rightly, concentrated on primary research to improve cancer care. Scant interest has been paid to how evidence is used. At ASCO (1998) there were 2199 abstracts, 55 were on health services – none reported on how to use data better.

**Methods:** Narrative reviews (NR) in general oncology and ovarian cancer were analysed and synthesised with descriptions of potential sources of bias when analysing evidence.

**Results:** 159 NRs tried to minimise bias in less than 10% of cases. Publication bias was due to poor searching (7%); failure or delayed publication of trials, language bias, not taming abstracts into papers, publication in obscure journals. These factors mostly effect "negative" trials. Multiple publication, often difficult to detect, conversely effects "positive" trials. Other failures include not writing a protocol (2%), not saying how quality was assessed (8%), how data were selected (6%) and how validity was assessed (7%). Data synthesis is most often qualitative (92%) and was rarely quantitative (5%).