In locally advanced stages III and IV long term survival is very much dependent on the (im-)possibility of achieving R0 resection. Attempts to improve results of surgery have been focusing on multimodality regimens mostly induction therapy. The majority of randomised trials using either chemotherapy or chemoradiotherapy have not been able to improve overall results. However mainly chemoradiotherapy is resulting in complete sterilisation on pathologic examination after esophagectomy in approximately 20%. This subset of patients seems clearly to benefit from multimodality treatment as compared to surgery alone with high 5-year survival ranging between 60-80%.

Because of difficulties in clinical staging of lymphnode involvement many centers until now have restricted indications for induction therapy to clinical T4 situations It is hoped that more precise staging modalities such as PET scan may offer better options in selection of candidates for induction therapy as well as for evaluating response with further refinement of patient selection for subsequent surgical exploration.

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Preoperative radiochemotherapy; experience from Dublin

Abstract not received.

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Preoperative radiochemotherapy; experience from FFCD-EORTC

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Surgery is standard treatment for localized resectable oesophageal cancer.

However the 5-y OS remains disappointing. Recurrences appear equally destributed between local and distant. The main objective of preop XRT-CT is to increase the local effect of radiation expecting that if local control is dramatically increase, then it could translate into a gain in survival.

Between 1/89 and 6/95, 297 patients with resectable squamous cell cancer of the thoracic oesophagus were enrolled into a FFCD-EORTC joint study that compared preop XRT-CT to surgery alone. The results have been previously published (N Engl J Med 1997; 337: 161-7). Patients in the preop group had more curative resection (0.017), lower TN stage (0.001), longer DFS (0.003), better local control (0.01) and lower cancer-related deaths (0.002). This major efficacy did not translate into improved OS, possibly due to more post-op deaths in the pre-op group (3.6% vs 12.3%). Multivariate analysis showed a better prognosis for patients with curative resection, tumour sterilization, no lymph node involvment based on CT-scan and distally located tumours.

Because the negative results on OS were possibly due to deleterious effects of non optimal radiotherapy, FFCD and EORTC are starting a new joint study comparing surgery to preop XRT-CT in which radiotherapy modalities have been reconsidered.

At this moment preop XRT-CT should still be considered experimental.

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Neoadjuvant chemotherapy in oesophageal cancer

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The outlook for patients with resectable oesophageal cancer remains poor. Neoadjuvant chemotherapy offers an opportunity to improve survival by potentially facilitating surgical resection and eliminating micro-metastatic spread. A number of randomised trials investigating neoadjuvant chemotherapy in OC have previously failed to conclusively demonstrate a survival advantage or not. However, the largest study of pre-operative chemotherapy in resectable OC has recently been reported by the MRC. 802 previously untreated patients were randomised to either two 4-day cycles, 3 weeks apart, of cisplatin 80mg/m2 and 5-fluorouracil 1g/m2/day by continuous infusion for 4 days, followed by resection (CS group) or resection alone (S group). In the CS and S groups respectively, median age was 63 and 62 years; 77% and 74% were male; 66% and 67% had adenocarcinoma and 65% and 63% had lower third tumours. Macroscopic complete resection was achieved in 78% CS compared with 70% S ($p<0.001$). In intent-to treat analyses, overall survival was better in the CS group (hazard ratio 0.79; 95% confidence interval 0.67-0.93; $p=0.004$). Median survival was 16.8 months CS compared with 13.3 months S and 2-year survival rates were 43% CS and 34% S. Post-operative complications were similar in both arms. There was no evidence of a different treatment effect according to histology, age, sex, site of tumour and weight loss. In the treatment of patients with resectable OC therefore, 2 cycles of pre-operative cisplatin and 5-fluorouracil improved survival without incurring additional adverse events. This MRC trial is the only neoadjuvant chemotherapy trial in OC, which has a hazard ratio with sufficiently narrow 95% confidence limits to one side of equivalence. It is therefore the only trial of neoadjuvant chemotherapy in OC, which has results, which can be interpreted with confidence. Since it represents a worthwhile benefit for patients with resectable OC, neoadjuvant chemotherapy with 2 cycles of cisplatin and 5-fluorouracil followed by surgery should become the standard treatment in trials in this patient group. New treatment approaches remain necessary to further improve outcomes, as is the need for clinicians to cooperate in entering patients into well designed randomised trials of neoadjuvant treatment in OC.

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After bone marrow transplantation

Abstract not received.

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Genetic risk factors for cervical cancer

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Cervical cancer is caused by infections by human papilloma virus (HPV). Epidemiological studies have indicated a RR=1.93 for first-degree relatives of cancer cases to develop cervical tumours. Studies of the heritability have shown that about 26% of the liability to the disease is due to additive genetic factors. Genetic factors can be postulated to exert their effect at a number of stages, ranging from exposure to HPV, infection, persistence of infection, sensitivity to viral oncoproteins and, finally, the rate of tumourigenesis. We have initiated a search for genetic susceptibility loci using a material of over 700 affected sib-pairs and 200 multi-case families identified through population-based registries. Three types of strategies are being employed in the search for susceptibility loci: a) evaluation of previously implicated candidate loci, such as HLA class I and class II loci and P53, and novel candidate loci, such as the cellular receptor for HPV, b) an unbiased search for susceptibility loci using a genome scan with 400 microsatellite markers, c) studies of the familial pattern of loss of heterozygosity (FLOH) in tumours. The status of these analysis and results obtained will discussed, as well as the potential for using genetic markers in risk assessment for individual women.

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Secondary malignancies in patients treated for sarcoma

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The problem of secondary malignancy in patients with sarcoma can be seen from two angles:

A) Not so rarely, sarcomas themselves arise as secondary malignancies. Bone sarcomas, in particular, are among the more frequent secondary cancers. They may be induced by previous radiation therapy and are also associated with a number of predisposing genetic conditions, most notably retinoblastoma. While secondary sarcomas were long believed to be almost universally fatal, there is now sufficient evidence that a curative approach employing multimodal therapy as for primary sarcomas is often warranted and may be successful.

B) On the other hand, there is a definitive risk of secondary cancer, including both leukemia and solid neoplasms, following treatment for sarcoma. Results from over 5000 sarcoma patients treated on protocols of the German Pediatric Oncology/Hematology Society GPOH place this risk at 3.2% at 10 years. Pediatric soft tissue sarcoma was associated with a particularly high rate of second malignancies in some series. While treatment related factors can be held accountable for some of the secondary cancers after sarcoma, predisposing conditions are, again, important. Many secondary cancers after osteo- or soft tissue sarcoma are those which are also seen in the Li-Fraumeni-syndrome, for instance other sarcomas, brain tumors, or breast cancer. Germline p53 mutations have been detected in some affected individuals. Patients with Ewing-tumors do not routinely fall into this category. There, very intensive treatment regimens have been associated with the development of hematologic neoplasms, particularly

myelodysplasia. The prognosis of secondary solid tumors seems to be better than that of secondary leukemias, which often carry unfavourable cytogenetic characteristics.

In summary, secondary sarcomas and secondary malignancies after sarcoma constitute a relevant threat, but neither are universally fatal. Therapy related induction as well as individual predisposition contribute to the development of multiple cancers in sarcoma patients.

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Overview of secondary cancer after childhood malignancies: Quality of data and general results

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Childhood cancer is rare affecting one in 500 live-born children before the age of 15. This implies that national or international populations in the order of 20 million inhabitants are required to reliably estimate the type-specific incidences of cancer in childhood and the relative risks of second malignant neoplasms among survivors in particular. Such large studies, which have been reported from the Nordic countries, the UK, the US and Japan, are reviewed and the general results and tendencies are presented. In particular, the most important similarities and differences are discussed. The relative risk of several types of second malignant neoplasms is markedly increased, however, in general with higher estimates found in hospital-based than in population-based studies. Methodological limitations in the hospital-based studies are though to be the main reason, although differences in treatment intensities of childhood cancer (e.g. between the US and Europe) also may play a role. Based on the population-based studies in particular the absolute excess risk of cancer in adulthood among childhood cancer survivors will be given. Special attention is devoted to a description of the risk of breast cancer among patients treated for Hodgkin's disease.

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Secondary leukemias and Lymphomas: what is the interest of individual dosimetry?

Abstract not received.