Results: Overall relapse rate in the patients group was 71/366 (19,4%). We analysed relapse rates in areas initially involved: out of a total of 1205 analysed areas, 11.4% showed the criteria of bulk, 1068 had lymphomas <7.5 cm. There was no difference in the two groups concerning the relapse rates in the initially involved nodal areas (8.6% (no bulk) vs 8% (bulk). The risk of local recurrence in the irradiated group with bulky disease was as low as in the (unirradiated) group without one. Recurrence free survival rates also showed no difference (77.3% (no bulk) vs 74.1% (bulk)). Regarding the whole group of patients with nodal disease, pts with bulky disease had a significantly shorter time to treatment failure than pts without bulk: three year recurrence free survival was 66.1% (no bulk) vs.53.3% (bulk).

Conclusion: The fact that in irradiated patients the poor prognostic factor "bulky disease" is not significant anymore supports the data from the literature that radiotherapy is an effective consolidation treatment in patients with aggressive NHL.

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Long term follow up of a randomised trial comparing local radiotherapy with wide field radiotherapy in stage I and II Hodgkin's disease

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Introduction: Between 1970 and 1979 a randomised controlled trial of involved field radiotherapy (IFRT) against extended field radiotherapy (EFRT) in patients with stage I and IIA Hodgkin's disease was undertaken by the British National Lymphoma Investigation (BNLI). In patients without B symptoms the comparison was between involved field and either mantle or inverted Y radiotherapy, in patients with B symptoms the comparison was between mantle or inverted Y radiotherapy and total nodal irradiation. With a minimum of 21 year follow up the results have been analysed for relapse-free and overall survival rates. 603 patients were randomised into this trial, median age 30 (range 15 to 78) of whom 363 (60%) were male. 433 (72%) had nodular sclerosing disease, 94 (16%) mixed cellularity, 68 (11%) lymphocyte predominant and 7 (1%) lymphocyte depleted. 220 (37%) had mediastinal involvement.

Results: In laparotomy confirmed stage I and IIA disease (n=332) there is a significant difference in recurrence-free survival between IFRT and EFRT. This difference is maintained across the prognostic groups even in very favourable patients female <40yrs with no mediastinal disease). The actual difference is 12% at 5, 10 and 15 years from initial treatment (p = 0.02). A similar but statistically non-significant difference is seen in the patients having no laparotomy (n=210) and in no group is there any effect between primary radiotherapy treatment and overall survival. In stage I and IIB disease no impact on recurrence-free survival or overall survival was seen between patients having IFRT and EFRT. Limited data on late toxicity in this group of patients shows no difference in rates of second malignancy between patients receiving IFRT and EFRT with an incidence of 13 and 14% respectively.

Conclusion: long term follow up of this trial confirms the recognised increased relapse rate in patients receiving IFRT compared to EFRT for early stage disease but no detrimental impact of IFRT on overall survival or advantage of IFRT in second malignancy rates is seen. The results from radiotherapy alone for patients with B symptoms are poor and justifies current practice using primary combination chemotherapy for these patients.

Head and neck cancer

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Prognostic Significance of COX-2 Expression in Advanced Head and Neck Cancer Treated with Radiotherapy in a Phase III RTOG Trial (90-03)

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Objective: To assess the impact of cyclooxygenase-2 (COX-2) expression on the outcome of patients with advanced head and neck carcinomas (HNC) treated with radiotherapy.

Methods: Unstained histologic slides were available from 154 of 268 analyzable patients randomized to the standard radiation arm of a Phase III RTOG trial (IJROBP 48:7, 2000). The slides were deparaffinized, rehydrated, blocked for endogenous peroxidase, and stained with polyclonal COX-2 antisera (PG-27b, Cayman Chemical). Immunoreactive complexes were detected using the standard ABC method and evaluated utilizing an immunohistochemical (IHC) scoring system for the intensity of staining (0: no, 1: weak, 2: moderate, and 3: strong staining) and the % of tumor cells staining positive (0: none, 1: 1-10%, 2: 11-50%, 3: 51-80%, and 4: 81-100%). These parameters, individually or combined (i.e., product of scores), were correlated with the clinical prognostic features and time to locoregional failure (TTLRF) or distant metastasis (TTDM), which were calculated using cumulative incidence method with testing by Gray's test. The median follow-up was 59.5 months for living patents.

Results: There were no significant differences in the T-stage, N-stage, tumor site, KPS, age, gender, and race or in the therapy outcome between patients with (n=154) and those without (n=114) COX-2 assessment. The frequency distribution by % cells stained was 0: 12, 1: 22, 2: 51, 3: 51, and 4: 12 and by staining intensity was 0: 18, 1: 3, 2: 47, and 3: 86. There was no significant correlation between the TTLRF and COX-2 expression. We found a significant correlation between the TTDM and the staining intensity (p=0.038 for 0-1 vs 2-3), the % of tumor cells stained (p=0.011 for 0-2 vs 3-4), or the combined scores (p=0.016 for 0-1 vs 2-12; p=0.039 for 0-3 vs 4-12).

Conclusion: This study showed that 88% of advanced HNC express COX-2, an enzyme playing a role in carcinogenesis and tumor response to therapy. No correlation was detected between COX-2 expression and the clinical prognostic factors but a there was a significant correlation between COX-2 expression and TTDM, which suggests that COX-2 expression is a useful independent prognostic determinant of distant spread. If confirmed by further study, COX-2 expression can serve as a patient stratification or selection variable for clinical trials addressing new or aggressive adjuvant therapy.

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Hypoxia and hemoglobin as prognostic markers of survival in head & neck carcinoma after primary radiation therapy. An international multi-center study

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Purpose: To assess the prognostic value of pretreatment oxygenation status in head and neck squamous cell carcinoma (HNSCC) after primary radiotherapy.

Methods: Tumor oxygen partial pressure (pO2) was measured by invasive electrodes (Eppendorf) in 321 stages III-IV SCCHN from 6 centers, n=267 male and n=54 female. Median age was 58 years (range 22-92). Nine patients with distant metastases had palliative treatment and 314 patients had a full course of radiation therapy alone or combined with surgery, chemotherapy or hypoxic sensitizer. Endpoints were overall survival (OS) and pO2 parameters were fraction of pO2 values<2.5 mmHg (HF2.5),<5 mmHg (HF5) and median tumor pO2 (mmHg).

Results: Inter-tumor variability was large as the median tumor pO2 ranged from 0 to 77 mmHg (overall median=10 mmHg). Both HF2.5 and HF5 ranged from 0 to 100% (median=20% and 29%, respectively). At 3 years follow up 192 patients were dead. By Kaplan-Meier analysis at 3 years HF2.5 and HF5 were prognostic for OS in all 314 patients (27% vs. 38%, p=0.005 and 31% vs. 35%, p=0.04, respectively) whereas median tumor pO2 was not significant (p=0.30). By multi-variate analysis HF2.5 and stage were significant independent prognostic variables of OS. Hemoglobin (Hb) data were available in 274 patients. Also Hb was a strong prognostic marker for OS (22% vs 39%, p=0.001) when devided by an over all median = 13.2 g/dl. There was no correlation between Hb and HF2.5, HF5 or median pO2, respectively. By multivariate analysis in this subgroup of patients Hb, HF2.5 stage and age were significant prognostic variables of OS.

Conclusions: This study showed that tumor hypoxia defined by HF2.5 adversely affected OS in advanced SCCHN treated by primary radiation therapy. Also, Hb was a strong prognostic marker of OS and apparently independent of HF2.5.