abovementioned findings and may facilitate a more limited and focused node dissection, avoiding dissection of unnecessary areas.

In conclusion, new knowledge in this field is challenging the standard lymph node staging procedures, i.e. obturator node dissection, as the sentinel nodes are often found farther away from the primary tumor site. To avoid extensive lymph node dissections with their concomitant morbidity, the novel techniques described will be useful, but further refinements will be necessary and are doubtlessly underway.

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Intra-arterial cisplatin and concomitant radiation for inoperable head and neck cancer

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Purpose: To determine the feasibility and effectiveness of intra-arterial cisplatin with concomitant radiotherapy (RADPLAT) for locally advanced, inoperable stage IV, squamous cell carcinoma of the head and neck.

Patients and Methods: From April 1997 to December 1999, eighty-five patients with locally advanced head and neck carcinoma were treated with radiotherapy (70 Gy, 7 weeks, 35 fractions) and concomitant supra-selective intra-arterial cisplatin (150 mg/m2, day 1, 8, 15, 22) and systemic sodium thio-sulfate rescue (RADPLAT). Main inclusion criteria were: inoperable squamous cell carcinoma of the head and neck or cancer requiring total glossectomy, any N, M0, Karnovsky performance status at least 60%, no prior surgery, radio- or chemotherapy. The median age was 50 year (40–69). Tumor characteristics: 75 patients had a T4 tumor, 10 T3, (3–10 cm), 61 had N+ disease, (1–10 cm).

Results: All patients received the scheduled treatment. Complete remission was achieved in 90%. At 40 months: Disease free survival, Locoregional Control and Local Control were 50%, 62% and 68% respectively. No treatment interruptions or dose limitations resulted from acute toxicity. One patient had a treatment-related death. Seventeen percent had grade IV (CTC) hematological toxicity, no other grade IV side-effects were seen. Grade III acute toxicity (RTOG): mucositis in 43%, upper GI in 60%, hearing loss in 10%.

Conclusion: The RADPLAT treatment schedule is feasible with excellent response rates and organ preservation. Based on the results of this study, a multicenter phase III trial comparing radiotherapy and concomitant systemic cisplatin versus RADPLAT is ongoing.

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Postoperative Combined Radiation and Chemotherapy Improves Disease-Free Survival (DFS) and Overall Survival (OS) in Resected Adenocarcinoma of the Stomach and G.E. Junction. Results of Intergroup Study INT-0116 (SWOG 9008)

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The cure rate for patients with resected gastric cancer is 5% - 40%. INT-0116 was designed to evaluate post-operative adjuvant chemoradiation in resected gastric cancer.

Study Design: Patients with stages Ib through IV M0 adenocarcinoma of the stomach or gastroesophageal junction who had undergone gastric resection with curative intent were randomized to postoperative follow up or chemoradiation. The treatment consisted of one cycle of 5-FU (425 mg/m*)/Leucovorin (LV) (20 mg/m*) in a daily x5 regimen followed by 4,500 cGy (180 cGy/day) given with 5-FU/LV (400 mg/m* and 20 mg/m*) on days 1 through 4, and on the last 3 days of radiation. One month after completion of radiation, two cycles of daily x5 5-FU/LV (425 mg/m* and 20 mg/m*) were given at monthly intervals.

Results: Between 8/1/91 and 7/15/98, 603 patients were accrued to this study, 47 (8%) of which were ineligible. Nodal metastases were present in 85% of cases. The combined modality regimen in this program was tolerable. There were 3 (1%) toxic deaths. Grade 3 and grade 4 toxicity occurred in 41% and 32% of cases, respectively. The gr. 3 toxicities were: hematologic (54%), GI (33%), infection (6%), neurologic (4%). OS and DFS analyses were based on intention to treat. With 3.3 years of median follow up, 3-year DFS is 49% for treatment and 32% for observation (p=0.001); 3-year OS is 52% for treatment and 41% for observation (p=0.03).

These results demonstrate a 44% improvement in relapse-free survival (hazard ratio of 1.44), and a 28% improvement in survival with median survival of 27 months in the observation arm vs. 42 months in the treatment arm (hazard ratio 1.28). Postoperative chemoradiation may now be considered a standard of care for high-risk R0 resected locally advanced adenocarcinoma of the stomach and GE junction.

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Radiochemotherapy is more effective than dose escalation in locally advanced head and neck cancer: results of a german multicentre randomized trial

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Purpose: Is accelerated chemoradiation more effective than accelerated radiotherapy alone?

Methods: Between March 1995 and May 1999, 384 patients with locally advanced H&N cancer were recruited for this multicentre study from 10 German centers. Male/female ratio was 82%/18%, mean age was 55 years. The oropharynx (60.4%) and hypopharynx (32.3%) were the predominant tumour sites, oral cavity tumours accounted for only 7.3% of all tumours. 5.5% and 94.5% of all tumours were stage III and IV, respectively. All patients with stage III- and IV-disease lacking evidence of distant metastases qualified for the treatment. Three target voumes (TV) were defined as follows: 1. Macroscopic tumour and lymph nodes 2. High-risk regions for lymphatic spread 3. Low-risk areas of lymphatic spread. The overall treatment time in both study arms was 6 weeks (40 days). The fractionation in study arm A was 14 Gy/2 Gy q.d. and b.i.d. 1.4Gy to a total dose of 77.6 Gy. Mitomycin C on days 5 and 36 @ 10mg/m* and 350 mg/m* 5-FU as bolus plus a 120 hrs. continuous infusion of 600 mg/m* 5-FU were additionally applied.

Results: The median follow-up was 30 months for all patients. The absolute values of locoregional failures in arm A vs. B were 49.7% vs. 37.6% (p=0.03). The total no. of metastases did not differ with 30.6% (arm A) vs. 34.9% (arm B). Actuarial locoregional control values were 46.4% (arm A) vs. 57.0% (arm B) @ 2 years (p=0.03). The hazard ratio (HR) was 0.72 (CI: 0.53-0.98). The overalll survival rates were 39.1 (arm A) vs. 49.4% (arm B) @ 2 years (p=0.05). The HR was 0.80 (CI: 0.62-1.04). None of seven parameters tested for acute grade 3 and 4 morbidity were statistically different in both treatment arms. Of 12 parameters tested for late grade 3- and 4 morbidity, only dysphagia (p=0.01) turned out to be pronounced in treatment arm A.

Conclusions: These results give evidence that accelerated radiotherapy of 70.6 Gy plus MMC/5-FU is superior to 77.6 Gy of accelerated fractionation alone in terms of locoregional control and overall survival at equitoxic levels of acute and late radiation morbidity.

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Concurrent chemo/radiotherapy in cervical cancer. What don't we know?

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Radical radiation therapy had been the accepted standard of care for advanced cervical cancer. In February 1999 the U.S. NCI issued a rare Clinical Announcement: "..five randomized phase III trials show an overall survival advantage for cisplatin-based therapy given concurrently with radiation therapy." "..strong consideration should be given to the incorporation of concurrent cisplatin-based chemotherapy with radiation therapy in women who require radiation therapy for treatment of cervical cancer."

The trials compared various doses and schedules of concurrent cisplatin-containing chemotherapy to pelvic irradiation alone, extended field irradiation or radiation and hydroxyurea. A similar reduction in the relative risk of death was observed. Absolute survival benefits ranged between 9 and 18%. These and other relevant studies including the two large randomised Canadian studies showing no detectable benefit will be reviewed.

The data suggest that the optimal regimens of concurrent chemoradiation are ill defined and may not be the "standard" of weekly cisplatin. A large study using oral 5-FU and Mitomycin has demonstrated benefit, as did one using Epirubicin. One study did not show benefit with concurrent infusional 5-FU when added to optimized radiation.

The Canadian study of pelvic irradiation with or without concurrent weekly cisplatin did not show survival benefit. The relative risk of death with concurrent therapy was 0.91. A number of possible explanations may