Methods: 81 patients (pts) with oral cavity cancer were treated with combined surgery and radiotherapy in the MSC Institute, branch in Gliwice, Poland between 1990 and 1997. There were 15 pts (18%) in T_1, 34 pts (43%) in T_2, 17 pts (21%) in T_3 and 15 pts (18%) in T_4 stage. Forty four patients had positive neck lymph nodes, i.e. 22 (27%)-N_1, 21 (26%)-N_2 and 1 (1%)-Nx. The risk of loco-regional recurrences and distant metastases was scored using Peters scale including tumour grading and margins, number of positive nodes, extracapsular invasion, vessels embolia. Radiotherapy was given in daily fractions of 2 or 1.8 Gy to total dose of 60 ÷ 70 Gy depending on the risk score. Neck nodes were electively irradiated with a total dose of 50 Gy and it was increased up to 60 ÷ 70 Gy depending on the risk score.

Results: Median follow-up was 28 months (2 ÷ 81 months). Surgery was macroscopically radical in 74 pts (91%) and non-radical or uncertain in 7 pts (9%). Loco-regional control was observed in 73 pts (90%), uncomplete control in 4 (5%). In the remaining 4 pts (5%) it was impossible to determine the effect of irradiation at the end of the treatment because of very severe mucosal reaction. Loco-regional recurrence was observed in 19 pts (23%), distant metastases in 2 pts (2%), mainly in those with non-radical surgery.

Conclusion: It seems that the precise determination of surgical macro- and microscopic margins and complete information concerning the risk of the loco-regional failure has an important impact on optimization of postoperative radiotherapy.

626 POSTER

Totally implantable venous access devices (TIVAD) and head and neck cancer. Results of a prospective and homogeneous series of 170 patients

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Introduction: Head and neck cancer is often observed in smoking and alcohol abuse patients. These particular patients with an important infectious risk (tracheotomy, dirty skin, bad hygiene) need a safe central venous access for chemotherapy and supportive care. TIVAD provide a good vascular access.

Materials: We carried out a prospective and homogeneous series of 170 patients treated between 01/94 and 12/98: 166 males and 4 females with a median age of 51 years old (range 37–67). All patients have a sqamous cell carcinoma stage III or IV. (38% recurrent, metastases). We used a Districath® (Districlass®) TIVAD.

Methods: All patients received the same regimen consisting of cisplatin 25 mg/m^2 d 1–4, fluorouracil 1000 mg/m^2 as continuous perfusion over 96 hours d 1–4 every 21 days (3 cycles) for neoadjuvant (103 pts), concomitant (3 pts), recurrent or metastatic (64 pts) chemotherapy. Others uses are: blood transfusions, perfusions. TIVAD were implanted by percutaneous cannulation of the subclavian vein after local analgesia under sterile surgical procedure.

Results: TIVAD is a good vascular access (failure of implantation 0%) for chemotherapy (continuous perfusion, bolus). We observed 0 intolerance, 0 infection, 0 septicemia during the treatment. The percutaneous implantation is a reliable and rapid technique with a light morbidity (0 death due to the method).

Conclusion: TIVAD used in head and neck cancer patients provide a reliable and safe venous access for chemotherapy and supportive care. They reduce the infectious risk and improve the security and quality of life of patients.

627 POSTER

Nasopharyngeal carcinoma with cranial nerve palsy

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Purpose: To evaluate various prognostic factors and the impact of imaging modalities on tumor control in patients with nasopharyngeal cancer (NPC) with cranial nerve (CN) palsy.

Methods: From Sep. 1979 to Dec. 1996, 313 NPC patients with CN palsy received radical radiotherapy (RT) in Chang Gung Memorial Hospital-Linkou. Imaging methods used varied over that period, and included conventional tomography (T) for 54 patients, computerized tomography (CT) for 228 patients magnetic resonance image (MRI) for 31 patients. Upper CN (II–VI) palsy was found in 249 patients, lower CN (IX–XII) in 13, and 51 patients had both. All patients had good performance status (WHO < 2). The RT was delivered by megavoltage or Co-60 X-ray. Therapeutic modalities did not change significantly over the 17-year study period. The median external RT dose was 70.2 Gy (63–74.6). Brachytherapy was also given to 146 patients in addition to external RT. It was delivered by the remote after loading high dose rate technique. 121 patients received cisplatin based chemotherapy before or after radiotherapy. Recovered from CN palsy occurred in 169 patients during or after radiotherapy. All the patients had been followed more than 2 years.

Result: The 3 year-overall survival was 45.8% and 5-year 30.6%. Patients who had undergone MRI study had better survival than those studied with CT scan or T study. 5-yr survival was 49.3%, 30.7% and 22.2% respectively. Patients with both CN palsy had worse survival than those with only lower CN or upper CN involvement. Patients who recovered from CN palsy had better survival than those who did not. The addition of brachytherapy decreased survival while an external RT dose of more than 70 Gy may improve the survival. The use of chemotherapy did not improve survival or tumor control in this study.

Conclusion: The use of more modern image study was associated with improved survival of patients with NPC causing CN palsy. Patients recovering from CN palsy had better survival. Giving more radiation dose via external beam may a better way to achieve tumor control rather than brachytherapy.

628 POSTER

Radiochemotherapy in the treatment of locally advanced head and neck cancer: Results after five years of a randomized study

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Purpose: This study was undertaken to evaluate the efficacy of two regimens of chemoradiotherapy in the treatment of locally advanced head and neck cancer.

Methods: From 1992 to 1997, 127 patients with locally advanced head and neck cancer (stage III–IV) were randomized. Sixty-six patients (group a), 42 male and 24 female, with a median age of 48 years (range 40–7) received during radiotherapy two course (1_{th}–6_{th} week) of chemotherapy with carboplatin (300 mg/m^2 day 1) and etoposide (60 mg/m^2 days 1 to 3). Sixty-one patients (group b) received two cycles of chemotherapy with 5 FU (750 mg/m^2 days 1 to 5) and MIT C (10 mg/m^2 day 1). The median dose of radiotherapy was 60 Gy (range 55–66 Gy) 180 cGy/d 5w.

Results: The actuarial five years survival rate (Kaplan-Meier) was 38% for group a (CBDCA + etoposide + RT) and 25% for group b (5FU + MIT C + RT). The difference was statistically significant (P = 0.036). Toxicity group a: mucositis G III in 41 patients and G IV in 16; disphagia G III in 46 patients and IV in 5; leukopenia in 24 patients.; 28 patients required nutritional therapy. Toxicity group b: mucositis G III in 38 patients and G IV in 17; disphagia G III in 48 patients and G IV in 3; leukopenia in 23 patients; 25 patients needed nutritional therapy.

Conclusions: The data of actuarial survival five years rate suggest that concomitant chemotherapy in group a (CBDCA + etoposide + RT) is better than concomitant chemotherapy in group b (5FU + MIT C + RT).

629 POSTER

Expression of p73 protein, a p53 homologue, in normal & malignant undifferentiated cells of head & neck malpigian epithelium

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In about 50% head and neck squamous cell carcinoma (HNSCC), there are *p53* mutations as well as occasional p53 nuclear accumulation (likely without mutations) in normal basal & parabasal cells of the peritumoral tissue (Ahomadegbe *et al., Oncogene* 1995). *P73* gene, with a high *p53*-homology in the DNA binding domain, encodes 2 isoforms differing by C-terminal splicing, p73α & β. *In vitro*, p73α induces *p21* gene transactivation and apoptosis. To investigate putative p73 involvement in malpigian epithelium carcinogenesis, immunohistochemical studies using a polyclonal antibody raised against a C-terminus α isoform epitope (a gift of D Caput, Sanofi, France) were performed on normal mucosa adjacent to 29 HNSCC (11 undifferentiated and 18 well differentiated).

Results: In normal malpigian epithelium, an intense and conspiscuous nuclear staining restricted to basal and parabasal cells as opposed to a total lack of staining in keratinized differentiated layers were consistentely observed. In 11 undifferentiated cancers, there is a homogeneous and diffuse staining in all tumor cells; in contrast, in 18 well differentiated tumors, all dif-

ferentiated malignant cells were negative whereas the basal undifferentiated cells located at the periphery of the carcinomatous clusters were positive.

Conclusion: Concomitant p21-p73 nuclear stainings strongly suggest that p73 expression i) is restricted to proliferafive compartment of the malpigian epithelium, ii) could be involved in HNSCC carcinogenesis.

630 POSTER

Microvascular free tissue transfer in craniofacial reconstruction after tumour resection

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Purpose: Microvascular free tissue transfer (FTT) is an invaluable adjunct for head and neck oncologic surgery. Together with advanced imaging techniques, better approaches to skull base tumors, and advances in craniofacial surgery, it allows resection of locally advanced tumors that were thought unresectable. In this study, different free flaps will be used for reconstruction of a variety of major cranial-facial defects that resulted from ablative surgery of deeply invasive tumors.

Methods: This study involves a total of 28 patients who had T3 or T4 head and neck cancers including the scalp, skull base, midface, oral cavity, and the mandible. These patients underwent extensive resection that resulted in large defects that were reconstructed using FTT from October 94 to January 1999. Sixteen patients at MD Anderson Cancer Center, Houston, Texas (from July 96 to July 97), and twelve patients at The National Cancer Institute, Cairo, Egypt. The success rate, recipient vessels used, complications were examined. The ultimate functional and aesthetic outcome of the free flaps were compared and discussed in relation to the site of reconstruction.

Results: Free flaps were used to reconstruct a variety of extensive craniofacial defects. These defects consisted of skull base (8), scalp (5), midface (5), oral cavity (5), and mandibular defects (5). Immediate reconstruction was performed in 25 patients, while 3 patients underwent delayed reconstruction. Free flaps used included rectus abdominis (10), latissimus dorsi (5), radial forearm (6), fibula (5), lateral thigh (1), and omentum (1). Eleven patients received preoperative radiation therapy. The most commonly used recipient artery was the external carotid artery (20), whereas the most commonly used recipient vein was the internal jugular vein (17). The free flaps were successful for 27 patients. One patient who underwent free omentum for scalp reconstruction developed partial flap necrosis. Salvage surgery was successful for one flap. There was no perioperative death. Two patients developed CSF leakage, which stopped spontaneously, a patient has cerebrovascular stroke, and 3 patients have minor wound complications.

Conclusion: Free tissue transfer is a realistic option for reconstruction of major craniofacial defects. After resection of cranial base tumors the rectus abdominis is an ideal flap for cranial base reconstruction. For composite scalp and calvarial defects free muscle flap covered with split thickness skin graft is ideal. In midface composite defects myocutaneous free flaps provide plenty tissues required for such three dimensional defects. The radial forearm flap is ideal for oral cavity reconstruction, whereas the free fibula is our preferred method for mandible reconstruction

631 POSTER

Chemotherapy and accelerated radiotherapy in head and neck carcinoma: The experience from four swiss centres

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Purpose: To give a critical appraisal of the experience with combined radiotherapy (RT) and chemotherapy (CT) from four single-institutional non-randomized studies.

Methods: Individual patient data were collected from 4 Swiss centers (BS, ZH, GE, VD) treating advanced head and neck cancers with RT (217 pts.) or RT + CT (182 pts.).

Results: Early toxicity was significantly increased after CT + RT compared with RT alone. Local tumour control was only improved in one center. However, there was a confounding effect of patient selection in all studies. Late complications were not registered systematically, and no definitive conclusions can be drawn for these.

Conclusion: Non-randomized studies are difficult to interpret in terms of tumour outcome because of the, often deliberate, selection of cases for RT + CT. Toxicity data are less subject to this selection bias. Nonrandomized studies may produce valuable insights. Still, a definitive evaluation of therapeutic efficacy requires a randomized-controlled trial.

632 POSTER

Prognostic significance of angiogenesis in squamous cell carcinoma of the larynx

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Purpose: A retrospective immunohistological study of biopsies of SCC H&N (T2/T3 NO larynx) from 26 patients that underwent curative radiotherapy (R/T) between 1990–1994 (55 Gy in 15 f over 3–4 weeks) was undertaken to investigate the role, and prognostic significance, of factors involved in regulating tumour angiogenesis.

Methods: The role of the novel cytokine EMAP II in the radiation response was investigated together with factors that play a direct role in the angiogenic process (VEGF and Flk-1). Mean vessel density (MVD) was assessed in tumour tissue, and accompanying stroma, using a mAb against PECAM-1 (CD31) to reveal endothelial-lined vessels.

Results: Correlates with patient's response to R/T indicate that a high MVD may be indicative of a high risk of tumour recurrence in that 87.5% of those patients with recurrences had MVD's $\geq$11.0 as opposed to 33% for those that did not have recurrences. There was no correlation between levels of VEGF, EMAP-II or Flk-1 expression and clinical outcome.

633 POSTER

Docetaxel (DTX) + cisplatin (CDDP) in locally advanced or metastatic head and neck cancer (HN). A phase II study

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Purpose: DTX is among the most promising new drugs in HN, while CDDP is acknowledged as probably the most active single agent. Since the combination of the two drugs has shown clinical activity in HN, we started a phase II study in patients (pts) with locally advanced and metastatic HN.

Patients and Methods: Eligible pts, never pretreated with chemo- (CT) or radiotherapy (RT), received a combination of DTX 75 mg/m^2 and CDDP 100 mg/m^2 every 3 weeks. After 3 cycles, pts were re-evaluated; responding pts with locally advanced HN underwent RT, while metastatic responding pts received further CT.

Results: 46 pts (median age 59; M/F = 39/7) were accrued. 45 pts had locally advanced disease, while 1 pt had lung metastases. 44 pts are evaluable for response. 4 complete responses (CR) and 16 partial responses (PR) have been observed, for an overall response rate of 45%, according to intention-to-treat analysis. In 2 pts with PR and 1 pt with SD after CT, a CR was achieved after subsequent RT. Neutropenia (grade 3–4 in 25 pts) and diarrhea (grade 3–4 in 5 pts) were the main side effects. 10 pts died before completion of 3 courses of treatment; in 6 cases (grade 4 diarrhea in 4, and neutropenic sepsis in 2) this was considered probably CT-related.

Conclusion: DTX + CDDP is an active, but toxic regimen in HN. Careful selection of pts is needed for further trials.

634 POSTER

Oral enzymes preventing side effects of radiation therapy in patients with head and neck cancers

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Based on in vitro data and on clinical evidence of a protective action against acute side effects of radiotherapy, a prospective randomised study was undertaken to determine the safety and efficacy of an oral enzyme combination in patients with head and neck cancer receiving conventional fractionated radiotherapy (Wobe-Mugos® E, MUCOS Pharma, Geretsried, Germany) (OE).