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

A. Amin[1], B. Baldwin[2], H. Meebed[3], M. Bassiouny[3], F. Amer[3], S. Hewidi, M. Schusterman. *[1]NCI, Surgical Oncology, Cairo, Egypt; [2]MD Anderson Cancer Center, Plastic and Reconstructive Surgery, Houston, Texas, United States; [3]NCI*

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

S. Bieri[1], S.M. Bentzen[2], P. Huguenin[3], C. Landmann[4], M. Monney[5], A.S. Allal[6], L. Cozzi[1], J. Bernier[1]. *[1]Cantonal Dept. of Radiation Oncology, Ospedale San Giovanni, 6500 Bellinzona, Switzerland; [2]Gray Laboratory Cancer Research Trust, Mount Vernon Hospital, Northwood, United Kingdom; [3]Dept. of Radiation Oncology of U.H. of Zurich; [4]Basel; [5]Lausanne; [6]Geneva, Switzerland*

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

S.G. Martin, S.M.T. Gama, J.C. Murray, N. Griffin[1], D.A.L. Morgan. *University of Nottingham, Dept of Clinical Oncology and Queens Medical Centre; [1]Dept of Histopathology, Nottingham, United Kingdom*

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

F. Caponigro, L. De Lucia, M. Biglietto, A. Avallone, F. Rivellini, C. Sguotti[1], L. Manzione, P. Comella, G. Mantovani, G. Comella. *Southern Italy Cooperative Oncology Group (SICOG) c/o National Tumor Institute of Naples, Italy; [1]Rhône-Poulenc Rorer, Origgio, France*

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

M.S. Gujral[1], P.M. Patnaik[2], R. Kaul[1], G.V. Daftary[3], H.K. Parikh[3], C.P. Tamhankar[3], W. Schiess[4]. *[1]SGPT Cancer Hospital, M. Y. Hospital Campus, Indore; [2]AH Regional Cancer Centre, Cuttack; [3]SIRO Research Foundation, Mumbai, India; [4]MUCOS Pharma, Clinical Research, Geretsried, Germany*

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).

Two study centres included 100 patients with locally advanced head and neck cancer into this open study. Radiation was delivered with telecobalt machines using standard daily radiation dose of 150–200 cGY in 30–35 fractions over a period of 6 weeks. Two lateral parallel opposing fields were used with the portal area generally being 4 × 6 inches. Patients were randomly allocated to two groups: Patients in the test group were given OE orally three times daily starting 3 days prior to radiotherapy and continuing up to 5 days after completing radiotherapy. Patients in the control arm were not given any drug.

The control group and the test group were comparable with respect to presenting features. In the test group the maximum severity and duration of mucositis, skin reaction, and dysphagia were significantly less as compared to the control group. The duration of these side effects as well as the sum scores of toxicity was also significantly less in the OE group.

In summary the use of OE with conventional fractionated radiotherapy was feasible without significant safety problems. There was a clinically relevant protection against acute side effects of radiotherapy in the OE group. Not only was the severity of acute side effects less but the duration was shorter and the time to onset was also delayed.

635 POSTER

The effect of cervical lymph node biopsy on distant metastases in carcinoma of the nasopharynx

N.-M. Tsang[1], P.-C. Pai[1], C.-K. Tseng[1]. [1]*Chang Gung Memorial Hospital, Department of Radiation Oncology, Kwei-Shan, Taiwan*

Purpose: To investigate whether the neck lymph node biopsy increases affects the rates of distant metastasis, neck recurrence, and survival in AJCC T1-3N1-3 nasopharyngeal carcinoma (NPC) patients.

Materials and Methods: We retrospectively analyzed the records of 543 patients with AJCC T1-3N1-3 NPC who had completed the recommended course of treatment (>=64 Gy total dose) and were followed up for more than 5 years. We compared the metastasis, neck recurrence, and survival rates in those with and without pretreatment node biopsy, and between excisional and incisional biopsy.

Results: No significant differences were found in terms of the rates of metastasis, recurrence, or survival in-patients with and without pretreatment biopsy. In addition, the method of biopsy and the time interval between operation and the start of local treatment did not significantly influence the outcome.

Conclusion: Our findings suggest that neck lymph node operation before local-regional irradiation does not increase the rate of distant metastasis in AJCC T1-3N1-3 NPC patients.

636 POSTER

Survival and organ preservation following surgical treatment for hypopharynx carcinoma

H.E. Eckel[1], M. Jungehuelsing[1], U. Schroeder[1], P. Volling[2], T. Betten[1]. [1]*Universitiy of Cologne, Department of Otorhinolaryngology, Head and Neck Surgery, Cologne;* [2]*Evangelisches Krankenhaus, Department of Otorhinolaryngology, Head and Neck Surgery, Oldenburg, Germany*

Background: Surgery, usually in combination with postoperative radiotherapy, is believed to provide highest cure rates in patients with hypopharynx carcinoma. However, the percentage of patients suitable for primary surgery, surgical mortality rates, and organ preservation rates for this routinely used therapeutic approach have not been studied in detail. This study seeks to evaluate treatment modalities, mortality following surgery, survival, and organ preservation for a consecutive cohort of unselected hypopharynx cancer patients treated according to a prospective protocol that favors surgery as initial approach to the disease whenever possible and ethically justifiable.

Material and Methods: The charts of 228 consecutive patients with previously untreated hypopharyngeal squamous cell carcinoma seen from 1986 to 1997 were reviewed. No patient was excluded from data analysis. Outcome measures were calculated using the Kaplan-Meier estimator. Surgery was offered as initial treatment if the primary tumor and regional metastases seemed completely resectable, distant metastases were not detected during preoperative work-up, coexisting malignancies did not preclude a curative approach, general health status of the patient was considered sufficient to withstand the operative trauma, patients were willing to undergo surgery, and were judged to be capable of dealing with the consequences of such treatment.

Results: Out of 228 consecutive patients, 136 (59.6%) were found suitable for initial surgical treatment. Of the remaining 92 patients, eighteen (7.9%) had nonresectable lymph node metastases, sixteen (7.0%) had unresectable primaries, thirteen (5.7%) refused surgery, thirteen (5.7%) presented distant metastases during initial diagnostic work-up, eight (3.5%) had coexisting primaries that precluded a curative surgical approach, twelve (5.3%) had severe cardiopulmonary disorders, nine (3.9%) had multiple risks excluding major surgical interventions, and three died prior to the initiation of any kind of therapy. Of those who had surgery, 46 had larynx sparing procedures, 54 total laryngectomy, and 36 total laryngopharyngectomy. Microvascular jejunum loops for pharynx reconstruction were used in 22 patients, and gastric pullup in 14. None of the patients who had surgery died postoperatively. Actuarial five year overall survival was 26.6% for all 228 patients, 35.9% for the 136 patients with surgical treatment, 59.3% for the 46 patients who were treated with larynx-sparing procedures, and 12.9% for those not treated surgically.

Conclusion: Only 59.6% of 228 unselected, consecutive patients were suitable for surgical treatment. For these, no postoperative fatalities were observed. Five year overall survival was significantly better for pa-tients who qualified for surgery (35.9% versus 12.9%), but only 27.5% of them had their larynx preserved after five years.

637 POSTER

Oral cavity squamous cell carcinoma in stage II with a high percentage of DNA content >5C cells, have a significantly short disease free survival

L. Santos, I. Costa, C. Palmeira, I. Azevedo, M. Lopes, L. Pontes, P. Lopes, C. Lopes, J. Guimarães dos Santos. *Portuguese Oncology Institute, Oporto, Portugal*

Purpose: In stage II oral cavity tumours, the classic clinical-pathological variables, have not allowed the identification of worst case prognosis. The outcome after standard treatment is not homogeneous, so it becomes important to identify the tumours that would benefit from a combined and aggressive therapy. The tumour suppressor genes and its products e.g. p16, p27, p53 and pRb, are involved in oral cavity carcinogenesis, representing part of the genetic instability and alterations of DNA content. These variables were used to identify stage II oral cavity squamous carcinomas with high risk of recurrence.

Methods: forty two patients with stage II oral cavity spinal cell carcinoma (AJCC), admitted and treated consecutively at the Portuguese Oncology Institute of Oporto (IPO) between January 1989 and December 1998, were evaluated for overall and disease free survival relating to the following variables: sex, age, alcohol and tobacco consumption, tumour size and grading, immunoreactivity for p16, p27, p53, pRb, Ki-67 and DNA content by image cytometry.

Results: Mean age of patients was 63.1 ± 10.4 years; 31 males and 11 females; median follow-up was 21 months (1–95 months); the most frequent location was the tongue (47.6%); only 16.6% of patients had no history of alcohol and tobacco consumption; 12 recurrences were observed (28.5%). Immunoreactivity was present for p53 (45.2%), p27 (66.6%), p16 (38.1%), pRb (47.6%), Ki-67 (90.4%). The aneuploidy was prevalent (83.3%); 19% of this cases had a high number (>17%) of tumour cells with DNA content >5c and a significantly short disease free survival rate ($p = 0.01$). The absence of immunoreactivity for p16 and pRb was the most frequent alteration of tumour suppressor genes products. The high rate proliferation cases (Ki-67 > 50%) were significantly related ($p = 0.008$) with absence of immunoreactivity for p27. Of all the variables studied only the aneuploid cases with a high percentage of DNA content >5c cells, showed a negative and significant correlation with disease free survival.

Conclusion: The high percentage of DNA content >5c cells, is a prognostic indicator in stage II oral cavity squamous cell carcinoma.

638 PUBLICATION

Improved results in the treatment of nasopharyngeal carcinoma using combined radiotherapy and chemotherapy versus radiotherapy alone

B. Baltalari[1], A. Aydin[2], M. Esassolak[2], A. Arican[2], D. Yalman[2], N. Dem Rbag[3], Y. Anacak[2], Z. Ozsaran[2], S. Oskok[2], A. Haydaro-Lu[2]. [1]*Pamukkale Un Versity, Radiation Oncology, Denizli;* [2]*Ege University, Radiation Oncology, Izmir;* [3]*A. Osman Sonmez Oncology Hospital, Bursa, Turkey*

One hundred and twenthyfour patients with locally advanced nasopharyngeal carcinoma who were treated in the department of radiation oncology in Agean University Faculty of Medicine between January 1986 and January 1996, were analysed retrospectively in order to evaluate the influence of combining chemotherapy (CT) and radiotherapy (RT) on survival rates: