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POSTER

Detection of cell surface sialylation of head and neck carcinomas by a new histobiochemical method

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Purpose: The sialoglycans and the degree of sialylation on the cell surface are of increasing interest because of the possible contribution to metastasis and invasion. Primary tumors and metastasis may differ in the degree of sialylation.

Methods: Cell surface sialylation of 30 lymph node metastases and 30 squamous cell carcinomas of the head and neck was determined by a new histobiochemical assay on cryostat sections which is based on the enzymatic introduction of a fluorescence-labelled sialic acid (CMP-9-fluoresceinyl-NeuAc) into lactosaminyl type (Gal β 1-4 GlcNAc) oligosaccharide chains of cell surface glycoproteins by α -2,6-sialyltransferase. To compare degree of sialylation with the total amount of sialylation sites a pretreatment with sialidase for desialylation was required.

Results: We observed a significant ($p = 0.001$) higher amount of lactosaminyl type binding sites for sialic acid on metastases compared to the primary tumors. Pretreatment with sialidase could detect a significant amount of sialylation on primaries and metastases, showing a lower degree of sialylation in metastases. In primary tumors no correlation was seen between the amount of binding sites and tumor localization, TNM-stage or histological grading of the tumors.

Conclusion: A higher degree of sialic acid free lactosaminyl glycans on the cell surface of head and neck tumors seems to be correlated with the occurrence of metastasis. Our new histobiochemical method turned out to be effective, reliable and little laborious.

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Complications rate following neutron or mixed beam irradiation for patients with head and neck malignancies

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Purpose: to review the incidence of complications following neutron irradiation for patients with malignancies of the head and neck region.

Materials and Methods: retrospective review identified 30 patients with malignancies of the head and neck region who received a minimum neutron radiation dose of 1000 NcGy. Neutron beam is produced by 48.5 MeV neutron \rightarrow Be reaction. Twenty-one patients were treated by neutron irradiation alone and received a median dose of 2040 NcGy (range 1700–2040 NcGy) delivered at a median fraction size of 170 NcGy (range 100–170 NcGy). Nine patients received mixed neutron and photon irradiation with median doses of 1050 NcGy (range: 1020–1360 NcGy) and 1980 cGy (range 1280–3400 cGy). Seven patients had undergone radical surgical resection of their tumor prior to the initiation of radiation therapy. Eight patients received concurrent cisplatin systemic chemotherapy during the radiation therapy course. Patients were followed for a median period of 20 months (range 5–61 months).

Results: The two year actuarial incidence of grade 3–5 complications for the entire group is 66%. Patients who received neutron irradiation alone, or mixed beam irradiation have a complication rate of 75% and 20% respectively. Concurrent chemotherapy and neutron irradiation was associated with a very high actuarial complication rate of 86% at two years. The corresponding crude complication rates are 40%, 52%, 11%, and 86%.

Conclusion: Neutron irradiation using similar beam energy and the dose fractionation regimen described above results in unacceptable high complication rate. This is particularly true if concurrent cisplatin is used.

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POSTER

Preliminary results of a randomised study using WR-2721 in radiation therapy alone in patients with head and neck cancer

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Purpose: Based on experimental and clinical evidence of radioprotection

of salivary glands using WR-2721 we started the prospective randomized study to verify these results.

Methods and Materials: Patients undergoing radiation therapy alone for carcinoma of the head and neck region were eligible, if minimal 75% of each parotid was in the treatment fields. WR-2721 (200 mg/m²) was administered prior to each irradiation. Assessment of adverse radiation reactions were performed. 22 patients were enrolled on the study in University Erlangen-Nürnberg up to 15.2.97.

Results: Administration of WR-2721 prior to each radiation dose was unproblematic. Radiation mucositis and dermatitis were equal in both treatment arms. The values of flow rates for whole saliva, stimulated parotid saliva and the excretion percentage of the parotid gland decreased markedly at 1–5 months posttherapy in both arms and we noted a residual function of parotid glands in the WR-2721 arm only.

Conclusions: Administration of WR-2721 at 200 mg/m² daily prior to irradiation was feasible without any relevant toxicity. In the first months after radiation therapy a residual function of salivary glands in the WR-2721 arm only were found.

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POSTER

Selective cytoprotection by amifostine (A) in the treatment of head and neck cancer with simultaneous radiochemotherapy (RCT)

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Purpose: A randomised study was conducted to evaluate the protective activity of A against the dose limiting toxicities of RCT.

Methods: Patients with head and neck cancer received radiotherapy (2 Gy/day 5 days a week to 60 Gy) with carboplatin 70 mg/m² on days 1–5 and 21–25 inclusive. Patients either received RCT alone ($n = 14$) or RCT and A at a dose of 500 mg prior to treatment with carboplatin ($n = 25$).

Results: There was a significant reduction in the incidence of grade 3/4 mucositis ($p < 0.0001$), acute grade 2 xerostomia ($p < 0.0001$) and grade 3/4 thrombocytopenia ($p = 0.012$) in those patients who received A. The incidence of grade 2 late xerostomia at 12 months is 16.7% and loss of taste is 0% in those patients treated with A compared to 54.5% and 63.6% in those patients who received RCT alone. There were 18 (72%) complete responses (CR) and 6 (24%) partial responses (PR) seen in patients who received A compared with 6 (43%) CR and 6 PR (43%) seen in patients treated with RCT alone. The disease free survival at 12 months is 85.7% in RCT + A arm and 78.6% in the RCT alone arm.

Conclusion: The use of A reduces the incidence and severity of acute and late toxicities associated with RCT whilst preserving anti-tumour activity.

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POSTER

Neoadjuvant chemotherapy with cisplatin (CDDP) plus 5-FU vs. cisplatin plus UFT in locally-advanced squamous head and neck cancer

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Purpose: In this study, the activity of Al-Sarraf scheme 5-FU+CDDP has been compared with the combination UFT + CDDP in neoadjuvant treatment of locally advanced head and neck cancer. Toxicity differences between the two schemes were also studied.

Methods: 67 patients with locally advanced head and neck cancer were distributed in a random manner into two groups. The first group received CDDP (100 mg/m²) on day 1, followed by a continuous infusion of 5-FU (1,000 mg/m²/d) on days 2–6. The second group received CDDP (100 mg/m²) on day 1, followed by oral administration of UFT (300 mg/m²/d) on days 2–20. Both treatments were started every 21 days and repeated 4 times. Responding patients received locoregional standard radiotherapy (50–70 Gy) after chemotherapy. The patient's characteristics were: Group 1: 34 pat. Sex: M/F: 30/4, Median age: 57.5 y.; P.S.: 90–100: 79.4%; 70–80: 20.6%. Histology: Squamous: 70.5%, Undifferentiated: 29.5%; Stage: III: 14.7%; IV (MO): 85.3%. Group 2: 33 pat. Sex: M/F: 29/4; Median age: 56 y.; P.S.: 90–100: 87.8%; 70–80: 12.2%. Histology: Squamous: 81.8%; Undifferentiated: 18.2%. Stage: III: 12.2%; IV (MO): 87.8%.

Results: In the first group the response rate was 73.5% (CR: 20.6%; PR: 52.9%) and in the second group the response rate was 81.2% (CR: 18.7%; PR: 62.5%). With a median follow up of 84 months, no significant differences

in overall survival (15 vs. 37 m.) ($p > 0.05$) and time to progression (8.5 vs. 14.5 m.) ($p > 0.05$) were found between the two groups.

Chemotherapy toxicity was not severe and similar in the two groups, except for febrile neutropenia which was significantly higher in the first group (88.2% vs. 9%).

Conclusion: The CDDP-UFT scheme was as effective as the CDDP-5-FU scheme in the treatment of locally advanced head and neck cancer, but produces a lower incidence of febrile neutropenia and avoids hospitalization.

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POSTER

Randomized trial of cisplatin (P) plus 5-fluorouracil (F) with or without folic acid in locally advanced head and neck cancer (LAHNC)

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P and F combination has been considered the standard as neoadjuvant treatment in LAHNC. Phase II studies have suggested an improvement in overall response with the addition of Folic Acid.

Method: From January 1995 to June 1996, 42 patients (pt) with LAHNC were included in a prospective randomized trial with two different arms. *Group A:* Neoadjuvant chemotherapy with P 25 mg/m²/day F 1000 mg/m²/day, both in a 96 hour continuous infusion. *Group B:* Identical schedule than group A plus Folic Acid 250 mg/m²/day in two hour infusion at the beginning of daily infusion of PF. In both groups 4 courses were administered, every 3 weeks. Both arms were balanced according to age, sex, stage and primary site. Most of pt were in stage IV.

Results: 39 pt were evaluable for response and toxicity. (3 pt in group B abandoned the treatment by own decision). Complete treatment (dose and number of courses) were administered in 71% of pt in group A and only in 44% of pt in group B due to toxicity. *Response:* Response Rate was 95% in group A and 94% in group B ($p = N.S.$). Complete Response in group A was 52% and in 39% in group B ($p = N.S.$). *Toxicity:* Main toxicity was grade III/IV neutropenia (29% in group A vs 46% in group B; $p < 0.1$) and grade III-IV mucositis (0% in group A vs 39% in group B; $p < 0.01$). Other grade III-IV toxicity was not observed.

Conclusion: In spite of both schedules are effective, addition of Folic Acid increases the toxicity leading to a lower compliance of the treatment without improvement in complete response rate.

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POSTER

Postoperative radiotherapy in squamous cell carcinoma of the larynx – Prognostic factors

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Purpose: An analysis of the results of postoperative irradiation for squamous cell carcinoma of the larynx and estimation of the influence of selected clinical and physical parameters influencing the efficacy of the treatment.

Methods: During the period 1986–1993, 272 patients with squamous cell carcinoma of the larynx were treated with surgery and postoperative radiotherapy. All patients were treated with ⁶⁰Co alone. The total tumor doses were in range 54–70 Gy, delivered by conventional fractionation. DFS rates were analysed according to: age, stage of disease, histological type, type of operation, surgical margin, total dose, the time-interval between surgery and irradiation, field size.

Results: At 3 years the DFS for the entire group was 53%. DFS was significantly influenced by: age (<40 = 4%, 41–60 = 66%, >60 = 30%), postoperative macroscopic evidence of disease ("–" = 65%, "+" = 40%), field size (<90 cm² = 33%, 91–120 cm² = 29%, >120 cm² = 38%).

Conclusion: It was found the age, macroscopic radical surgery and field size could be an important prognostic factors for combined surgery and RT for larynx cancer.

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POSTER

Laryngeal cancer T₃N₀M₀: Variations in organ-preservation treatment

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Purpose: To study the expediency of organ-preservation treatment of the larynx cancer T₃N₀M₀.

Methods: We studied 233 pts with squamous cell carcinoma of the larynx. The average age was 56. The following organ-preservation therapy was applied. 1. Hyperfractionated irradiation (single dose 1.1 Gy 2 times a day with 4 hours interval for 5 days a week, split course, total dose 70 Gy) – 76 pts. 2. Chemoradiotherapy (2 cycles of chemotherapy 5FU, CDDP, leucovorin and hyperfractionated irradiation, split course, total dose 70 Gy) – 67 pts. 3. Conservative surgery (larynx resection) – 90 pts.

Results: Alive without relapses and metastases (5 years) with larynx preservation was as follows: 1 group – 56.6%, 2 – 82%, 3 – 60%. Local relapses: 38.2%, 9%, 20%. Regional metastases: 2.6%, 6%, 16%. Distant metastases: 2.6%, 3%, 3.3%. Additional surgery of local relapses and regional metastases helped achieve 79% 5-years survival, which approximated the response of traditional laryngectomy.

Conclusion: We confirm the expediency of organ-preservation treatment for T₃N₀M₀ larynx cancer.

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POSTER

Estimation of the influence of biological modifiers on severity of acute mucosal reaction in patients with head and neck cancer

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Purpose: Estimation of the local efficacy of 2%AgNO₃ and dexamethasone-solution on severity of acute mucosal reaction during oral cavity and oropharynx radiotherapy.

Material and Methods: 107 patients with head and neck cancer in stage T₂₋₄N₀₋₁ were treated by radiation therapy alone in 2 schedule: accelerated with escalation of fraction dose and conventional continuous irradiation -CAIR (7 × 2Gy per week). The stimulation of buccal mucosal membrane in patients treated by accelerated schedule was performed by 2% AgNO₃ but patients treated in conventional continuous fractionation washed oral cavity by steroid-solution.

Results: The difference in acute mucositis intensity between stimulated and unstimulated buccal mucosa was highly significant with regard both to maximum score or duration. Intra oral washing by steroid solution during the radiation treatment diminish the intensity of mucositis chiefly to heal phase and gives better subjective tolerance.

Conclusion: Severity of acute radiation mucositis could be diminish by different mechanisms which are discussed. Both 2%AgNO₃ and steroid-solution improve acute radiation reaction tolerance and allow to realize planned accelerated irradiation in majority of patients.

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Neoadjuvant chemotherapy before radiotherapy of advanced head and neck cancer in Ukraine

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The records of 322 patients with advanced (M0) squamous cell carcinoma of the head and neck treated from 1983 till 1994 at Lviv Regional Hospital (Ukraine) were reviewed and divided in two arms. Arm I – radiotherapy alone (254 patients) 55-70 Gy, 2 Gy per fraction, 5 fractions a week. Arm II – 2 or 3 cycles of chemotherapy d1 -d21 (d28), with CDDP 100 mg/m² IVP d1, 5FU 1000 mg/m² d1 to d5 in 18 h continuous infusion, followed 15 to 21 days later by the same radiotherapy protocol. The arms were balanced by age, sex, stage, TN-classification, localisation of primary and dose of radiotherapy. Overall response was respectively 77% and 79%, 4-years survival 20% and 25%, but no significant. The results of multivariate analysis of patients from arm I, detected two prognostic groups of patients: group A – all women, men with III stage of disease (all localisations) and IV stage with incidence of primary tumor in nasopharynx and maxillary sinus; group B – only men with IV stage and localisation of primary in oropharynx and oral cavity. Group B has worse survival ($p = 0.0001$).

Use of neoadjuvant CT + RT in analogous group to group B permitted to improve complete response from 11.9% to 21.1% and overall Kaplan Meier survival from 7% to 26% (logrank $p = 0.02$) when compared with only radiotherapy in group B.

Conclusion: chemotherapy with CDDP-5FU does not improve the benefit of head and neck carcinoma treatment comparatively to radiotherapy alone. The advantage is possible only in men with IV stage and localisation of primary in oropharynx and oral cavity.