

st IV were significant (I + II v IV, III v IV, $p < 0.02$). FDM: st I v II v III v IV: 100% v 84% v 76% v 51% pts (Ho): I + II v III v IV: 100% v 91% v 69% pts (UICC). Both classifications show a difference ($p < 0.01$) in the comparison with st IV (I v IV, II v IV, III v IV). For Ho, a difference st I v III ($p < 0.03$) was also found. The "N" category is the main factor which influences FDM in both classifications: N 0 v 1 v 2 v 3: 100% v 84% v 68% v 51% pts (Ho); 100% vs 84% vs 73% vs 53% pts (UICC). All comparisons between N categories were significant ($p < 0.01$) in Ho's classification, while N1 v N2 was not significant for UICC.

Conclusions: Ho's classification represents a useful complementary tool to UICC classification for NPC, because: 1) Ho's classification is more accurate in describing differences in S and DFS between st I, II v III, 2) N categories, as defined by Ho, demonstrate the prognostic role of the involved node level in the occurrence of distant metastases. 3) Distribution among different stages is better balanced for Ho classification.

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POSTER

Comparative estimation of local control in radiotherapy supraglottic and glottic cancer

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Purpose: Comparative estimation of radiocurability in both groups of cancers localised in upper and medium level of larynx.

Material and Methods: From 1985 to end 1989 544 patients with cancer of larynx were treated with primary radiotherapy. There were 388 patients with squamous cell supraglottic cancer and 156 patients with glottic cancer. The total dose was in range of 59–80 Gy.

Results: The 5-year local control in supraglottic cancer was 74% and 82% for glottic cancer. TCD for 50% probability, of local control (TCD₅₀) for supraglottic cancer were: 61.5 Gy (T₁₊₂), 66.5 Gy (T₃) and 69.5 Gy (T₄). There were lower TCD₅₀ values for glottic cancer: 55.5 Gy (T₁₊₂), 63 Gy (T₃).

Conclusion: Higher radiocurability signs early glottic cancer T₁₊₂ (TCD₅₀ = 55.5 Gy) comparatively to supraglottic cancer T₁₊₂ (TCD₅₀ = 61.5 Gy). The same 50% probability of local control for T₃ glottic cancers is connected with Total Dose higher than in T₁₊₂ of 7.5 Gy and for supraglottic cancer higher of 5.0 Gy. For the same 50% probability of local control supraglottic cancer T₁₊₂ it is necessary to support Total Dose by about 6.0 Gy more than in glottic cancer T₁₊₂ and in T₃ supraglottic cancer by about 5.0 Gy more than in glottic T₃ cancer.

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POSTER

Is there any use in accelerated and hyperfractionated radiotherapy in locally advanced head and neck cancer?

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Purpose: In order to overcome accelerated tumor repopulation during radiotherapy a progressively accelerated hyperfractionated regimen was assessed for locally advanced head and neck cancer with initial poor prognostic factors.

Method: The treatment started with small field tumor volume with a conventional fractionation of 20 Gy in 10 fractions. This was followed by large fields by 1.66 Gy twice daily of 49.8 Gy for a total dose of 69.8 Gy. 104 patients with advanced head and neck cancer were treated. The oropharynx and larynx were the main localisations. The majority had stage III and IV tumors.

Results: After irradiation, a local control was obtained in 78/104 (75%) patients. Ten patients were salvaged with surgery after radiotherapy. During the observation period, 8 additional patients had a local relapse, thus the overall longterm control was 65%. Only 4 patients did not finish treatment because of severe acute toxicity.

Conclusions: The treatment schedule gives promising results. Shortening of treatment time certainly has its advantages. In discussing the results more emphasis will be given to a detailed analysis of early and late complications.

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POSTER

Differential expression of mRNA in squamous cell carcinoma of the head and neck

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Purpose: Nowadays carcinogenesis is considered a multistage process involving many genetic alterations. Differential display is a recently developed technique that allows the detection of differentially expressed mRNA from different sources. The identification of differentially expressed genes in malignant cells may further elucidate the process of tumorigenesis.

Methods: RNA from oropharyngeal and laryngeal keratinocytes, and squamous cell carcinoma cells of the larynx and the hypopharynx was extracted and reverse transcribed. PCR was carried out with 26 arbitrary decamer primers and cDNA was separated electrophoretically. Differentially expressed bands were cloned and sequenced and a genebank search was carried out.

Results: Currently 7 differentially expressed DNA fragments in the squamous cell carcinoma cells were identified, cloned and sequenced. Four of these differentially expressed fragments did not show any homology with known human, animal, bacterial or viral gene sequences. The remaining three fragments did show a homology of up to 98% with known but not further characterized human gene sequences.

Conclusions: These differentially expressed genes or gene fragments may represent formerly unknown oncogenes and may help to better understand the multistep procedure of carcinogenesis in head and neck cancer.

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POSTER

Sarcomas of the nasal cavity and paranasal sinuses

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Purpose: To analyse our experiences in treating nasal and paranasal sarcomas in adults, and to identify patterns of failure and prognostic factors.

Methods: 38 patients with Stage M0 disease treated by radiotherapy with or without surgery between 1960 and 1992 were analysed. Median follow up time was 71 months (range: 4–319 months). Local advanced tumors dominated: T1: 1, T2: 0, T3: 10, T4: 27 patients. Regional lymph node involvement was observed in 4 patients. Surgical excision was possible in 23 cases, but complete resection with negative surgical margins was achieved in only 6 cases.

Results: The calculated 5- and 10- year locoregional control-, cause specific survival- and disease free survival rates were 50%, 57%, 45%, and 50%, 48%, 45%, respectively. In case of combined therapy (surgery and radiotherapy) 5- and 10- year disease free survival rates were 69% and 51%, respectively. All patients with negative margins are under local control, 4 of them for over 13 years. In contrast we found poor results for patients with high-grade lesions and infiltration of the sinus sphenoidalis with 5- and 10- year locoregional control rates of 38%, 25% and 26%, 26%, respectively.

Conclusion: A combined treatment (surgery and radiotherapy), especially with radical surgical resection, should be the treatment of choice, because it offers the best chance for cure.

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POSTER

Changes in tumor oxygenation in split course radiochemotherapy (RCTH)

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Purpose: The importance of oxygen as a modifying factor in radiation therapy was already described by Gray in 1961, but clinical data are still rare. Our study presents clinical data about the oxygenation of tumors during RCTH (70 Gy, 5-FU, Mitomycin) and the influence of the oxygenation on the response of tumors.

Methods: Oxygen partial pressure (pO₂) was measured in 32 patients with advanced carcinoma of head and neck using a pO₂-histograph (Eppendorf, Germany). The clinical tumor response was quantified by measuring the tumor volume using ultrasonography. The time points of measurements were before RCTH, after first course of RCTH, after a two-week break of RCTH and at the end of RCTH.

Results: The oxygenation of tumors decreased during the first cycle of RCTh and increased during the two-week break, followed by a maximum decrease of the pO₂-value during the second course of RCTh ($p = 0.004$). The initially measured median pO₂-value was a good parameter to predict tumor response to RCTh ($p < 0.01$). Follow-up of the first 10 patients who were measured from March 94 to February 95 suggest that a good oxygenation (mean pO₂-value) after the two-week break correlates with a better prognosis ($p = 0.02$).

Conclusion: Preliminary results show that the initial oxygenation of the tumors as well as the reoxygenation during a fortnight break influence the tumor response to RCTh.

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POSTER

Randomized clinical trial of continuous accelerated irradiation (CAIR – 7 days a week) for head and neck cancer. Preliminary treatment results

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Purpose: Evaluation of preliminary (2-year) treatment results of 7 days a week continuous accelerated irradiation (CAIR) in compare to conventional radiotherapy

Methods: One hundred and one patients with squamous cell carcinoma of oral cavity, oro- and hypopharynx and supraglottic larynx in stage T2–4 N0–1 M0 were randomized between 2 groups: A (CAIR) – 52 pts and B (control) – 49 pts, and treated by radiation therapy alone in 1994–96. In majority (81%) there were the patients with advanced clinical stage (T3+T4). Irradiation technique and volumes, total and fraction doses were exactly the same in 2 groups of patients. Only the overall treatment time was shorter by about 2 weeks in CAIR group comparing to control because of the lack of weekend breaks.

Results: Ninety-eight patients (98%) completed the whole designed radiotherapy. Generally, 2-year local tumour control rate (LTCR) in CAIR arm was 85% and in control arm 40% ($p < 0.0001$). In aspect of tumour localization and stage the LTCR was significantly higher in CAIR arm than in control and was respectively as follows: 75% vs 26% in oral cavity, 86% vs 36% in oropharynx, 88% vs 50% in hypopharynx and supraglottis; 100% vs 64% for T2, 94% vs 39% for T3 and 66% vs 26% for T4. There were 14% of grade III and IV radiation morbidity in CAIR arm and 4% in control arm.

Conclusion: The high effectiveness of CAIR fractionation reflects the net effect of exclusion treatment weekend breaks and shortening the overall treatment time by 2 weeks.

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POSTER

Prognostic significance of irradiation of the posterior cervical lymph nodes in radiotherapy of oral cancer

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Purpose: We examined retrospectively if the inclusion of the posterior cervical lymph nodes (PCLN) in the planning target volume improves prognosis after radiotherapy of cancer of the oral cavity.

Patients and Methods: 188 patients were evaluated. 139 of them had been treated postoperatively (57 with inclusion of the PCLN, 82 without), 49 primarily (32 with PCLN, 17 without). These groups were evaluated separately. All patients were treated using lateral opposing portals in shrinking-field technique. Total dose to the primary varied mainly from 60–82.8 Gy (single dose 2×1.2 or 2.0 Gy), the dose to the PCLN varied from 30 to 60 Gy. Mean follow-up was 3.1 years.

Results: There was a bias between the groups towards a lower N-classification in patients whos PCLN had not been irradiated. Nevertheless, we never experienced a progression in the posterior cervical region during follow-up. In both groups locoregional tumor outcome, overall survival, progression-free survival and lymphoma-free survival were identical. Applying COX regression hazard model the dose to the PCLN never was an independent prognostic factor.

Conclusion: We think that radiotherapy of the PCLN can be omitted when there is no proven tumor involvement in the posterior neck triangle.

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POSTER

Inhibited expression of fibronectin in laryngeal squamous cell carcinoma cell lines

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Purpose: Molecular studies conducted on cell lines have demonstrated numerous alterations concerning the expression of different genes. A method called arbitrary primed PCR allows to detect changes in gene expression and does not require the construction of cDNA libraries. Aim of this study was to search for differences in the mRNA expression profiles of laryngeal squamous cell carcinoma (SCC) cells and normal keratinocytes from mucosa of the upper aerodigestive tract.

Methods: Total RNA was isolated from both cell types and reverse transcribed. cDNA was incubated with 0.2 μ M of one of 26 decameric arbitrary primers, 0.2 μ M of the corresponding anchored oligo (dT) primer, 2.5 μ M dNTPs, 1.5 μ M MgCl₂, 2 μ Ci ³³P-dATP, and 2.5 U Taq-polymerase in a final volume of 50 μ l. PCR was then conducted as described previously. After electrophoresis transcripts of interest were recovered from the gel and cloned into plasmid vector for sequence analysis.

Results: Selective expression of a 191 bp mRNA fragment was detected in normal keratinocytes. Although the sequence represented only a part of the mRNA including 3' poly (A) end, database search revealed a 99.4% homology with human fibronectin gene.

Conclusion: Fibronectin plays an important role in cell attachment due to its high affinity to the cell surface. Inhibition of fibronectin expression on mRNA level may be one of the molecular mechanisms involved in carcinogenesis. The absence of this adhesion molecule on the surface of the tumor cells may give an explanation for the phenomenon of missing contact-inhibition which is characteristic for cancer cells.

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POSTER

Cyclin-D1-expression of oral squamous carcinoma in comparison to precancerous lesions and normal oral mucosa

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Purpose: Cyclin D1 (CD1) is one of the important molecules in G1 restriction point control of the cell cycle. In a number of tumors, and especially preneoplastic lesions, amplification of the related gene or increased protein expression have been found. The aim of the presented study was the quantification and assessment of distribution pattern of CD1 this tissues.

Methods: 127 biopsies from 70 patients were stained with a three-step immunoperoxidase protocol using the anti-CD1-clone DCS-6 (DAKO). Quantification was carried out with a true colour image analysis system (CBA-8000, Leitz), data were gathered in Excel 5.0 and consequently analysed with SPSS ($\alpha \leq 0.008$).

Results: Significant differences were found between tumors grade 1 and grade 2 with high average values for CD1 in comparison to tumors grade 3 with mostly low or negative values for CD1. Further, no significant differences were found between normal lesions, leukoplakias and dysplastic lesions with mostly low values for CD1, and a distribution pattern of positive cells mostly confined to the suprabasal layer in the epithelium.

Conclusion: In oral squamous lesions CD1 seems not to be involved in tumor initiation as it has been shown for breast cancer. However, it may play role in tumor progression as is indicated by high values in well and moderately differentiated tumors. Whether the negative values in low differentiated tumors are related to a negative feed back after retinoblastom gene mutation will be pursued in our studies.

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POSTER

MIB-1 and ploidy in head & neck cancer (SCC H&N)

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Purpose: To determine whether the immunohistochemical expression of proliferation associated antigens (Ki-67/MIB-1) and DNA-aberration (DNA Index, ploidy) in addition to tumor volume are predictive for relapse-free survival (RFS).