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Influence of severe anemia on tumor oxygenation in squamous cell carcinoma of the head & neck (SCCHN)

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Purpose: To investigate the relationship between polarographically measured tumor oxygenation and Hb concentration in patients with SCCHN.

Patients and Methods: 114 patients with histologically proven SCCHN underwent pretreatment pO_2 measurements with an Eppendorf-pO_2 histograph. Measurements in healthy sternocleidomastoid muscles were made in 59 patients. The patients were divided into three groups according to their Hb level – severe anemia (Hb < 11.0 g/dl), mild anemia (female: Hb 11.0–11.9 g/dl/male: Hb 11.0–12.9 g/dl) and normal Hb (f: ≥ 12 g/dl/m ≥ 13 g/dl).

Results: No significant difference in tumor oxygenation could be detected between mildly anemic patients and normemic patients. Both, the proportion of values ≤5 mmHg and the median pO_2 in the severely anemic group were significantly below that of each of the other two groups ($p < 0.005$). There was no significant difference between the three Hb groups in the normal muscles.

Conclusion: A low hemoglobin concentration is associated with an inadequate oxygenation of malignant tumors and thus for an increased radioresistence. Consequently, a pretreatment correction of the Hb level as well as the maintenance of a sufficient Hb level during therapy could be a meaningful way to improve the oxygenation status of tumors.

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CT-assisted brachytherapy (BT) planning for nasopharyngeal cancer (NPC)

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Purpose: We reported excellent local control rates in NPC using external beam radiotherapy (ERT) and BT delivering cumulative doses up to 95 Gy (JCO 1998; 16: 2213–22), with local relapse-free survival of all tumor stages being 86% at 3-yrs. Aims of the current study were a) to use CT-images to determine the geographic accuracy of the *Rotterdam* tumor tissue (TT)- and normal tissue (NT) dose reference points (Radiother. Oncol. 1997; 45: 95–8), and b) to compare these dose reference points with a CT-assisted optimized dose distribution.

Materials and Methods: In our institution NPC is treated with ERT to a dose of 60 Gy (T1, 2a) or 70 Gy (T2b-4), followed by BT. In 15 study patients CT-scans were obtained with the nasopharyngeal applicator in situ. The target volume and critical normal structures were contoured and the dose optimized to lowest dose on target, using a 3D treatment planning system (Plato-BPS v. 13.3). TT coverage and dose distribution to NT, using both dose prescription methods, were correlated with pre- and post-ERT tumor extension.

Results: Target coverage using the *Rotterdam* TT- and NT dose reference points was found to be adequate in tumors staged ≤T2a (n = 5). For tumors staged ≥T2b (n = 10) and/or showing extension beyond the confines of the nasopharynx proper after ERT to a dose of 70 Gy, CT-assisted optimized BT treatment planning improved target coverage substantially.

Conclusion: In view of its ease of application and the highly conformal dose distribution, BT is the modality of choice for boosting small NPC. To improve target coverage for tumors ≥T2b, CT-assisted treatment planning is mandatory.

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Phase I-II study with docetaxel (D), cisplatin (C) and 5-fluorouracil (5-FU) in patients (pts) with locally advanced inoperable squamous cell carcinoma of the head and neck (SCCHN)

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The safety profile and activity of the combination of D, C and 5-FU was determined in 48 pts with locally advanced inoperable SCCHN. They were treated with D and C as a 1-hour infusion followed by a continuous infusion of 5-FU during 5 days every 3 weeks up to 4 cycles whereafter they were treated with locoregional radiotherapy (RT). Doses in level I were 75 mg/m^2 of D, 75 mg/m^2 of C and 750 mg/m^2/d of 5-FU and in level II the dose of C was escalated to 100 mg/m^2. Due to infectious complications in the first 18 pts, ciprofloxacine (cipro) was added from day 5 to day 15.

So far, 21 pts in level I and 14 in level II could be evaluated. At level I, 11 pts completed treatment and 9 pts at level II. 2 pts died due to infectious complications. Important side effects were neutropenia, infection, asthenia and renal toxicity, which were more pronounced in level II. Before introduction of cipro, 3 of 13 pts in level I and 2 of 6 pts in level II developed neutropenic fever leading to hospitalization. After adding cipro, 0 of 7 pts in level I and 0 of 6 pts in level II developed such complications. Response evaluation in 29 evaluable pts showed an overall response rate or 76%. All pts were treated with RT without unexpected toxicities.

Combination of D, C and 5-FU is highly active in pts with SCCHN. Cipro decreased infectious complications. Level I is the recommended regimen for phase III testing. An update of 25 patients treated in level I and 23 pts in level II will be available at the time of the meeting.

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Pretreatment hemoglobin (Hgb) is associated with response to neoadjuvant chemoradiation therapy (CRT) in patients with oral cavity and oropharynx cancers (OC&OP SCC)

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Objectives: Determine whether Hgb at the start of neoadjuvant CRT is associated with locoregional tumor control and overall survival of patients with T2–T4 oral cavity and oropharynx squamous cell carcinomas.

Methods: 116 patients were treated on a neoadjuvant CRT protocol in Vienna from 1990–1996 consisting of radiation therapy (50 Gy/33 days), mitomycin C (15 mg/m^2, Day 1) and 5-FU (750 mg/m^2/Day 1–5). Tumor resection and neck dissection were performed 4–5 weeks after CRT. Hgb was measured 1–3 days before neoadjuvant treatment.

Results: Hgb at the start of neoadjuvant treatment was <14.5 g/dL in 85 patients and >14.5 g/dL in 31 patients. The 2 groups did not differ significantly in T- or N-stage, age or sex distribution. Complete pathologic response to neoadjuvant treatment was achieved in 48% patients with Hgb > 14.5 g/dL and in 14% patients with Hgb < 14.5g/dL ($p < 0.001$). 3 year locoregional control (LC) was 90% in patients with Hgb > 14.5 g/dL and 71% in patients with Hgb < 14.5 g/dL ($p = 0.02$). 3 year overall survival (OS) was 84% in patients with Hgb > 14.5 g/dL and 64% in patients < 14.5g/dl ($p = 0.03$).

Conclusions: Pretreatment Hgb is associated with response to CRT, LC, and OS in patients with T2-T4 OC&OP SCC.

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Cell surface molecules in head and neck tumours

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Purpose: To screen various tumour markers in head and neck tumours.

Methods: To use immunocytochemical staining with monoclonal antibodies (Mab) for screening malignant and non-malignant tissue specimens from more than 100 of cases.