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The reconstruction of the lacrimal ducts in the cancer of the eyelids and the medial angle of the eye

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Purpose: Skin cancer located in the region of the medial angle of the eye, on the medial part of the upper and lower eyelids infiltrates and eventually closes the lacrimal ducts, which causes the leaking of tears onto the cheek.

Methods: In the years of 1997–99, in five patients, apart from the reconstruction of the eyelids, the outflow of tears was made by drilling a hole in the lacrimal bone through which a drain (/ 3 mm) was introduced to connect the conjunctival sac with the nasal dactule. The drain was removed after ten days.

Results: The ambulatory examination showed good cosmetic effects, and confirmed that tears flow out through the natural way to the nasal dactule. These results were also confirmed by the contrast examination.

Conclusion: Connecting the conjunctival sac with the nasal dactule by drilling a hole in the lacrimal bone is a good way of construction of the outflow for tears in the advanced cases of carcinoma of the eyelids and skin of the medial angle of the eye.

Radiobiology

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Alkyl-lysophospholipids activate the SAPK/JNK signaling pathway and enhance radiation-induced apoptosis

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Alkyl-lysophospholipids (ALPs) represent a new class of anti-tumor drugs that induce apoptosis in a variety of tumor cell lines. Although their precise mechanism of action is unknown, ALPs primarily target the cell membrane where they inhibit signaling through the mitogen-activated protein kinase (MAPK) pathway. Since stimulation of the stress-activated protein kinase (or c-Jun N-terminal kinase; SAPK/JNK) pathway is essential for radiation-induced apoptosis in certain cell types, we tested the effect of ALPs in combination with radiation on MAPK/SAPK signaling and apoptosis induction. We present data showing that three clinically relevant ALPs (Et-18-OCH3, HePC and the novel compound D-21266; ASTA Medica AG) induce time- and dose-dependent apoptosis in the human leukemia cell lines U937 and Jurkat T ($ED_{50} \sim 8\ \mu M$). Moreover, in combination with radiation, ALPs strongly enhance the induction of apoptosis, reaching levels of 80% after 16 h. All tested ALPs not only prevented MAPK activation, but, like radiation, stimulated the SAPK/JNK cascade 5–10 fold within minutes. A dominant-negative mutant of c-Jun inhibited radiation- and ALP-induced apoptosis, indicating a requirement for the SAPK/JNK pathway. Our data support the view that ALPs and radiation cause an enhanced apoptotic effect by modulating the balance between the mitogenic, anti-apoptotic MAPK and the pro-apoptotic SAPK/JNK pathway.

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Improving anti-cancer therapy by targeting the tumour vasculature with combretastatins

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Purpose: Combretastatins are a new class of tublin binding agents that appear to have anti-tumour activity by specifically damaging the tumour vasculature. The aim of this study was to investigate the potential of the lead compound, combretastatin A-4 disodium phosphate (CA4DP), to improve the effect of conventional anti-cancer therapies.

Methods: A C3H mammary carcinoma grown in the right rear foot of female CDF1 mice was used when tumours had reached to 200 mm^3 in size. We combined single radiation or hyperthermia treatments with CA4DP. Radiation response was determined by the TCD50 dose (radiation dose producing local tumour control in 50% of treated animals) 90 days after treatment. Thermal response was estimated by the tumour growth time (TGT; time taken for tumours to grow to 5× treatment volume) after heating at 42.5°C for 60 minutes

Results: The TCD50 dose (95% confidence interval) for control tumours was 52 Gy (50–55) and this was significantly decreased ($p < 0.05$) to 46 Gy (42–49) if mice were i.p. injected with 250 mg/kg CA4DP 30 minutes after irradiation, but only to 50 Gy (46–54) with 100 mg/kg CA4DP. The mean (±S.E) TGTs for tumours given either no treatment, 250 mg/kg CA4DP, or heat alone were 6.6 days (±0.5), 8.0 days (±0.6) and 12.8 days (±0.8), respectively. Injecting 250 mg/kg CA4DP 30 minutes prior to heating significantly increased the TGT to 15.6 days (±0.6). This thermal enhancement was independent of the drug dose from 25 to 400 mg/kg.

Conclusion: Radiation and hyperthermia therapy can be enhanced by combretastatins, but the drug-dose dependencies are different.

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Intratumoral microvessel density predicts local failure of radically irradiated squamous cell cancer of the oropharynx

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Purpose: To determine the predictive value of the intratumoral microvessel density (IMD) and expression of vascular endothelial growth factor (VEGF) for the radiocurability of pts. with squamous cell cancer of the oropharynx.

Methods: From 10/91 until 12/98 116 pts. with squamous cell cancer of the oropharynx were radically irradiated in our department. 151 paraffin embedded biopsies were analysed by immunohistochemistry (anti-CD31 for IMD, anti-VEGF). IMD was determined in hot spot areas at 200× magnification. VEGF expression was semiquantitatively determined (0, +, ++, +++).

Results: Increasing IMD (range 54–282) was strongly correlated with local failure as shown by multivariate Cox regression analysis (IMD as continous variable; $p = 0.0002$), whereas VEGF expression (0/+ vs. ++/+++; $p = 0.3347$) was not. When the IMD was categorized into 4 groups, the risk ratio for local failure increased from 2.71 (80–110) to 4.55 (111–130) and 13.01 (>130) compared to the base line group (<80). Moreover, pts. with PR or progression during radiotherapy had a significantly higher mean IMD than pts. with relapse after CR or pts. with continous CR (127.2 vs. 110.8 vs. 100.0; $p = 0.02$). There was no correlation between IMD and VEGF expression (Wilcoxon rank sum).

Conclusions: IMD is a strong predictive factor for treatment failure in radically irradiated squamous cell cancer of the oropharynx.

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Magnetic resonance perfusion imaging correlates with tumour oxygenation but not angiogenesis in carcinoma of the cervix

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Purpose: To compare the relationship between magnetic resonance (MR) perfusion imaging parameters, tumour oxygenation and vascularity in carcinoma of the cervix.

Methods: Gadolinium enhanced MR imaging was performed in 15 patients with stage Ib–IIIb carcinoma of the cervix prior to treatment and repeated in eight of these patients following 40–45 Gy external beam radiotherapy (EBT). Time/signal-intensity curves were generated and the average maximum signal intensity increase over baseline (SI-I) and rate of uptake over time in two regions of interest within the tumour were calculated. Tumour oxygenation measurements were performed in all 15 patients using the Eppendorf pO2 histograph system prior to treatment and repeated in eight of the patients following EBT. A pre-treatment punch biopsy was taken and immunohistochemically stained with CD31/CD34 for endothelial cells.