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Computerized analysis of angiogenesis (CD31) in invasive cervical carcinoma: Multivariate analysis

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Purpose: To evaluate the value of microvessel counts (MVC), as expressed by CD31 (sensitive endothelial cell marker), in invasive human cervical carcinoma.

Methods: Tissue sections of 134 patients with an invasive cervical carcinoma (FIGO I–IV) were stained with CD31. MVC were done using an image analyser in 10 fields. The results were compared with clinical-, pathological data and long time follow-up.

Results: Multivariate analysis gave this best model: vascular permeation, FIGO stage, tumor differentiation and MVC ($p < 0.001$).

Conclusion: Analysis of MVC with a computer is possible and provides significant data.

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Angiogenesis and biology – Correlation in liver tumors

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Purpose: Angiogenesis is indispensable for tumor growth, however, do the grade of vascularity and the malignant potential correlate to each other? We investigated the immunohistochemical study for the relationship between angiogenesis and biology of hepatocellular carcinoma (HCC), metastatic liver tumor and its primary site.

Methods: Twenty surgical resected specimens of HCC, 23 of metastases and their primary sites were examined. To evaluate angiogenesis, vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), factor VIII related antigen were used. Ki-67 antigen was used to evaluate for the cell proliferation. The expression of mutant-type p53 protein, bcl-2 (the apoptosis-inhibitor protein) and matrix metalloproteinases (MMPs) were analyzed.

Results: The expressions of angiogenic factors of HCCs were significantly greater than those of metastases, however, the levels of cell proliferation of metastases were higher than those of HCCs. Positive expression of VEGF in HCCs correlated with that of bcl-2 and MMP. Positive expression of p53 and bcl-2 in metastases correlated with higher level of cell proliferation.

Conclusion: Angiogenesis of HCC thought to be implicated in various biological factors.

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Angio-genesis-inhibition and intra-arterial chemotherapy – A new modality treatment for advanced and metastatic pancreatic carcinoma

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Introduction: Pancreatic cancer is resistant to most chemotherapeutic regimes and the results for improvement of quality of life and survival are dismal. The pattern of metastatic spread is largely defined to the upper abdominal organs within the arterial supply of celiac axis leading us to the use of intra-arterial chemotherapy in order to reach high regional drug concentrations. Due to the fact that pancreatic tumor cells over express growth factors contributing to tumor aggressiveness we tried to inhibit angio-genesis using low-dose *suramin* and *tamoxifen as a combined treatment.*

Patients and Methods: 28 consecutive patients with advanced pancreatic cancer (UICC stage III 7, stage IV 21) were treated by a minimum of two cycles of chemotherapy via an angiographie catheter in the celiac axis. 20 out of 28 patients were pretreated by surgery, chemotherapy and/or radiotherapy. Karnofsky performance status was 100 in 2 pts., 90 in 3 pts., 80 in 13 pts., 70 in 7 pts. and 60 in 3 pts. Out of 28 patients (male 10, female 18) 21 had liver metastasis. The schedule consisted of two different parts:

1. Angio-genesis inhibition by low-dose *suramin* 200 mg i. v. per week, *tamoxifen* 30 mg twice a day.

2. i.a. chemotherapy 210 mg *paclitaxel* over three hours on day one, 50 mg *cisplatinum* over 60 minutes on day two, 1500 mg *5-Fluorouracil* over 24 hours on day one and two, 7500 mg *treosulfan* over 60 minutes on day three. Treatment free interval was 28 days.

Results: According to WHO criteria there were 1 CR, 3 PR leading to re-operation and resection and 6 PR (remission rate of 36%). In 14/26 patients there was a stabilisation in disease (8/28 MR, 6/28 SD) with an improvement in quality of life and reduction of pain symptoms. Grade 3/4 hämatologic toxicity was observed in 6 out of 28 patients, Grade 2/3 gastrointestinal in 10 of 28 patients, alopecia in 10 of 28 patients, 1 patient up to now died due to complete caval thrombosis and another patient by acute hepatic failure. 6 months survival rate is 82%.

Conclusion: This pilot study shows that the combination of chemotherapy and inhibition of angio genesis is effective in the treatment of pancreatic cancer combined with a low rate of side effects.

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High correlation of the expression of p53 protein in synchronous head and neck and esophageal neoplasms

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Head and Neck and oesophageal mucosas have been described as a same field of cancerization. TP53 gene mutations have been described in both localizations. The aims of this study were to analyze the expression of p53 protein in a cohort of patients with synchronous neoplasms of the esophagus and head and neck neoplasms and to study the eventual correlation for p53 status between the two neoplasms for each patient.

Patients and Methods: 34 patients (median age: 61.52, sex ratio: 32/2) have been studied. All of them had synchronous squamous cell carcinomas of the esophagus and the Head and Neck. We have analyzed p53 protein expression by immunochemistry using murin antibody DO7 (Dako Laboratories).

Results: p53 overexpression was found in 25 cases (74%) for the esophagus and in 26 cases for the Head and Neck neoplasms. A correlation for the expression of the two localizations for a same patient was found in 27 cases (80%).

Conclusion: p53 overexpression seems to be a frequent event in esophageal and Head and Neck neoplasms. A high rate of patients have a concordance in the expression of p53 for the two localizations. These results seem to confirm the theory of "field of cancerization" but a prospective study with comparison to mutation analysis is probably necessary.

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Effect of amifostine (Ethyol®) on vascular density of the area vasculosa of chick embryos

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Purpose: Amifostine (Ethyol®) is used as a radioprotector. We studied the effect of this drug in a normal proliferating tissue to find out whether or not the development of the extraembryonic tissue is influenced.

Materials and Methods: For this study fertilised crossbred 'White-Plymouth-Rocks x Sussex' eggs were incubated in an upright position in a commercial incubator at 36.8 ± 0.1°C and 60–65% relative humidity. The daily weight loss of the eggs was 0.3 ± 0.05 g per day which was considered to be within the normal range. The eggs were incubated in air (20.9% oxygen). After 48 hr of incubation, the egg shell was opened and either 25 μg or 50 μg amifostine dissolved in 50 μl saline were injected below the inner shell membrane. The eggs were investigated by videomicroscopy, the video was analysed for vascular density (microvascular count, MC). At the end of the experiment tissue specimen were taken and analysed for PCNA (proliferating cell nuclear antigen).

Results: Within 20 hr after application an increasing number of blood islands were found in the treated part of the area vasculosa compared to the control side. These blood islands are significantly more numerous. Furthermore, after another 24 hr a significant increase in MC was observed. These results are confirmed by the results from immune histochemical investigation of PCNA.

Conclusion: Amifostine obviously induces vasculo- and angiogenesis in the normal area vasculosa of the chick embryo. This indicates that this drug may interfere with the up-regulation of genes encoding for growth factors.