

**2nd INTERNATIONAL CONGRESS
ON GASTROINTESTINAL ONCOLOGY**

ABSTRACTS

1 METASTATIC NEOPLASMS TO THE ORAL CAVITY

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Out of all cases of malignancies only 5% occur in the oral cavity. Metastases of malignant tumors to the oral cavity are not frequent and they represent 1-2% of the total number of malignancies of the oral cavity. Nearly all types of cancer metastasize to the orofacial region but more frequent are lung, breast, prostate, kidney, and liver cancer. Mainly the mandible is involved and less often the maxilla.

Our aim is to present the cases of two male patients, examined in the Dental Department of our Hospital. The first patient had ulceration on the right side of the tongue, for a month, without signs of improvement although topical treatment was prescribed. Second patient had a tumor on the edentulous part of the right side of the mandible with an ulceration of the oral mucosa, which was thought by the patient to be an injury caused by the flange of the partial removable denture. In both cases panoramic radiographic examination was performed and also biopsy samples were taken from the area affected. In both of them the histopathologic result was metastatic carcinoma with liver as the primary site.

Concluding, we must note that on one hand the low frequency of the metastatic neoplasms to the oral cavity makes the diagnosis a challenge for the general dentist and on the other hand certain "innocent" findings in the oral cavity should not be bypassed, as they could easily be the first clinical manifestation of a malignancy with unknown primary site.

Key words: cancer, metastasis, liver, mandible, oral mucosa, tongue

2 CAPECITABINE (XELODA®) USE AS RADIOSENSITIZER DURING PALLIATIVE RADIOTHERAPY FOR ADVANCED OESOPHAGEAL CANCER

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Introduction: Chemotherapeutic drugs that perturb nucleotide metabolism have the potential to produce substantial sensitization of tumor cells to radiation treatment. The clinical effectiveness of fluoropyrimidines as radiosensitizers has been proven in multiple randomized trials.

Methods: This study is aimed to present our experience of capecitabine (Xeloda®) oral use as radiosensitizer during palliative radiotherapy for advanced oesophageal cancer. Five patients, three males, two females with advanced inoperable oesophageal cancer were included in this study. All patients received external radiotherapy by Co-60, at the total dose of 5000cGy in 25 days (200cGy daily), using a four-fields technique (anterior and posterior opposing esophageal, left and right lateral). During radiotherapy all patients were administered 500mg capecitabine orally, 4 caps twice daily, after haematological and blood chemistry results, which were normal.

Results: Both patients showed significant objective tumor response to radiotherapy (computed tomography follow-up 3 months after radiotherapy showed 50% tumor reduction in comparison to initial size). Except for mild diarrhea in 2/5 patients no other severe side effects due to capecitabine administration or radiotherapy were reported. Six months later all patients are alive.

Conclusion: According to the results of this study, although great number of patients is needed, we consider that the oral use of capecitabine as radiosensitizer, enhanced the antitumor activity of radiotherapy also for advanced oesophageal cancer and may be potentially helpful in the treatment. However, further studies are necessary, the preliminary nature of this phase I study

3 PALLIATIVE ENDOSCOPIC INTERVENTIONS FOR OESOPHAGEAL CANCER: 5-YEAR EXPERIENCE

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Objective: To assess the value of endoscopic palliative management of patients with oesophageal cancer who either due to advanced stage of the disease or co-morbidity are unsuitable for surgery.

Methods: Retrospective review of all the endoscopic palliative procedures performed in a 5-year period in our Unit. The characteristics of the tumours, the degree of dysphagia, the type of palliation, the complications and the overall survival were recorded.

Dilatation and insertion of self-expandable metal stents (SEMS) were mainly used for tight circumferential strictures whilst laser ablation with neodymium-yttrium-aluminum-garnet (Nd: YAG) was used for exophytic or bleeding lesions. More than one session and combination of techniques was often necessary. All procedures were performed under sedation.

Results: Overall 249 palliative procedures were performed in 59 men and 40 women, with a median age of 73 years (range 35-93 years). The median number of palliative endoscopic sessions per patient was 2 (range 1-13 sessions). Palliation involved laser ablation alone in 24%, stent insertion alone in 22% and dilatation alone in 13% of the patients. In 41% of the patients, a combination of the above palliative techniques was applied. A total of 45 SEMS were inserted. One third of the patients did not receive any other palliative treatment, whilst the rest received chemotherapy, radiotherapy or chemoradiotherapy.

Swallowing was maintained in all patients up to death. Four oesophageal perforations were encountered; two were fatal whilst the other two were successfully treated with covered stent insertion and conservative treatment.

The median survival from diagnosis was 10.5 months (range 0.5-83 months) and median survival from 1st palliation was 5 months (range 0.5-68.5 months). The median time from diagnosis to first palliation was 3 months (range 0-47.5 months).

Conclusions: It is possible to adequately palliate almost all cases of malignant dysphagia. This is achieved by expertise in combination treatment. Endoscopic interventions are effective and relatively safe palliative modalities for patients with oesophageal cancer.

4 ANALYSIS OF LOCAL RECURRENCE AFTER OESOPHAGECTOMY FOR OESOPHAGEAL CARCINOMA.

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Background: The causes of local recurrence after oesophagectomy for cancer are usually regarded as inadequate surgical margin, multiple lesions, and residual intramural metastasis. However, there have been few reports on detailed analysis of local recurrence after oesophagectomy. We have analysed factors that may cause local recurrence after oesophagectomy.

Patients and Methods: There were 51 cases of autopsy performed after oesophagectomy for oesophageal carcinoma. Forty-three patients had curative resection. The clinicopathological and autopsy findings of the patients were reviewed and analysed.

Results: Thirty-five of the 51 patients (68.6%) had cancer spread at autopsy. The mode of cancer spread was local recurrence in 27.5% of the 35 patients with recurrence, lymph node metastases in 52.9%, hematogenous metastasis in 49.0%, and serosal carcinomatosis in 31.4%. One patient had cancer-positive proximal margin at operation, so this patient was excluded from the following analysis. Twenty-six percent of the 50 patients with cancer-negative proximal margin at operation had local recurrence at autopsy. The frequency of local recurrence was 0% in tumour located in cervical oesophagus, 33.3% in upper thoracic oesophagus, 19.2% in middle thoracic oesophagus, 23.1% in lower thoracic oesophagus, and 66.7% in abdominal oesophagus. The frequency of local recurrence was 22.2% after subtotal oesophagectomy with two-field lymphadenectomy, 14.3% after three-field lymphadenectomy, and 66.7% after lower oesophagectomy. The frequency of local recurrence was 20.0% in T1 tumour, 28.6% in T2, 15.4% in T3 and 50.0% in T4. The frequency of local recurrence was 30.0% in tumours within 3 cm from the proximal margin, and 23.3% in tumours over 3 cm from the proximal margin; however, there was no statistical difference.

Conclusions: Local recurrence after oesophagectomy may have correlation with tumour location, type of operation and T factor. Local recurrence was observed even in tumours with wide proximal margin. Subtotal oesophagectomy with two- or three-field lymphadenectomy may be recommended for advanced oesophageal carcinoma even when the tumour is located in lower oesophagus.

5 AN EFFECTIVE SURVEILLANCE PROGRAMME FOR BARRETT'S OESOPHAGUS IN A DISTRICT GENERAL HOSPITAL;

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Aim: To review the effectiveness of an endoscopic surveillance programme for patients with Barrett's oesophagus (BO).

Methods: All patients with BO over the period January 1997 to October 2002 were identified from endoscopic and histological records. 2 yearly surveillance endoscopies with quadrantic biopsies at 3cm intervals were performed in patients with classical Barrett's oesophagus (>3cms histologically proven columnar lined oesophagus). Patients with lesser lengths of BO, significant co-morbidity or age over 75 years were excluded. Dysplasia when identified led to repeat endoscopy at 3-6 weeks if high grade (HGD) or 3-6 months if low grade.

Results: 121 patients (24%) entered the surveillance programme of 505 patients identified with BO over the 70 month period studied. 205 endoscopies were performed for surveillance with a mean period of surveillance of 3.5 years. 65% entered remained in the surveillance program as of Oct 2002. The mean age at diagnosis was 60.2 years with male predominance (69.5%) and a mean length of Barrett's mucosa at the initial endoscopy of 7.5cms. 5 cases of HGD and 2 cases of adenocarcinoma were detected during surveillance. One patient with HGD refused surgery and died 2 years later of carcinoma oesophagus. The repeat biopsies in 3 of the 4 remaining patients who initially had HGD showed frank adenocarcinoma. Preoperative CT scans were clear of local or metastatic spread. These 6 patients underwent radical oesophagectomy and 5 of the 6 resected specimens showed early (T1,N0) adenocarcinoma with the other showing HGD. All patients remain well and tumour free after 24 months (mean, range 13 to 52 months). No interval oesophageal cancers occurred.

6 GASTROINTESTINAL STROMAL TUMORS (GIST). CLINICAL EXPERIENCE

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During the last decade immunohistochemistry has made GIST one of the most interesting tumors. GIST the silent tumor is the most common sarcoma among the gastrointestinal tumors (1%). It is originated from the interstitial cell of Cajal. GIST arises from the stomach (65%), the small intestine (25%) and the remaining (10%) from the colon, rectum, esophagus, mesentery, omentum or retroperitoneum. GIST usually is detected incidentally but in other cases the patients have symptoms such as pain or discomfort or dysphagia (esophagus) and obstructive jaundice (periampullary). About (25%) of the patients have bleeding from their tumors and in some cases they may appear with gastrointestinal bleeding or intraperitoneal hemorrhage. Obstruction of the intestine by a GIST is very common.

Objective: We want to present our experience during the last 10 years treating patients with GIST.

Patients-Methods: In this period (1995-2004) we have treated five patients with GIST. In three of the cases the tumor's origin was the stomach and in the other two the small intestine. The patients ages were between 55 to 72 (median age 63,2) and three of the were men two women. Two of those cases were discovered during gastroscopy for epigastric pain, the other two incidentally during CT scan for other reasons and the last case during our examinations for the cause of anemia and positive Mayer – test. All the patients were checked with CT scans for metastasis. During gastroscopy in one of the patients biopsy was unsuccessful because of bleeding.

Results: One of the patients positive for metastasis and was referred to an oncological center for treatment. All the other were treated surgically. All of them were treated with segmental resection of the stomach or the intestine (3 stomach – 1 intestine). All were c-kit positive tumors in pathologic examination and all the patients were referred to an oncological center for post operative treatment with ST 1571. CT scans are performed every six months for recurrence. Three of the patients are until now free of disease, while one of them presented with a recurrence and treated again with ST 1571.

Conclusion: GIST is the paradigm of molecular therapy since the c-kit proto – oncogene was discovered and ST 1571 was developed. It's a tumor amenable to treatment but in all cases a coordinated effort is required by pathologists, oncologists and of course surgeons.

7 TOLERANCE OF EARLY POSTOPERATIVE ENTERAL NUTRITION IN PATIENTS UNDERGOING MAJOR GASTROINTESTINAL SURGERY

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Clinical studies of the last 10 years support that early postoperative enteral nutrition (EN) improves the outcome after major gastrointestinal operations in terms of reduced morbidity, costs and length of hospital stay. However, early intra-gastric feeding usually is not well tolerated, whereas surgically placed feeding jejunostomies may be accompanied by serious complications. The aim of this study was to evaluate whether patients undergoing major gastrointestinal surgery tolerate early EN, using a manually placed nasojejunal feeding tube during laparotomy.

Methods: Thirteen consecutive patients with gastric, pancreatic and colorectal cancer were prospectively studied. During laparotomy, enteral access was provided by manually guiding a nasoenteric feeding tube through the nose and esophagus, into the first centimeters of the jejunum. EN, using a formula enriched with arginine, omega-3 fatty acids and RNA, began in the morning of the first postoperative day at a rate of 20 ml/h which was gradually increased to the target rate, and continued until the 5th postoperative day. The main outcome measures were tolerance of enteral feeding (amount of EN received over the amount needed to receive to meet energy requirements), and gastrointestinal dysfunction.

Results: The nasoenteric feeding tube was successfully placed in all the patients of the study, without any complication. Seven patients (53.8%) received 100% of the prescribed energy for the entire 5-day postoperative study period. Six patients received > 50% of their estimated energy requirements during the whole study period. Reasons why EN was interrupted or delayed included feeding tube clogging (1 patient), feeding tube dislodgment (1 patient) and abdominal distention and cramps (2 patients).

Conclusion: Our results show that early postoperative enteral nutrition by a nasoenteric feeding tube is well tolerated in the majority of patients undergoing major gastrointestinal surgery; this method of early postoperative feeding is simple, safe, and it can successfully substitute jejunostomy.

8 EXTRA-ADRENAL ABDOMINAL PARAGANGLIOMAS

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Objective: Extra-adrenal paragangliomas are rare tumors. We describe the clinical and pathological findings in 4 patients with paragangliomas of the omentum, duodenum, renal pelvis and retroperitoneum.

Materials and Methods: Between January 1999 and January 2005, extra-adrenal paragangliomas were diagnosed in 4 patients: 1 male and 3 female. The mean age of our patients was 53.25 +/- 17.34 years. We present the clinical data. Urinary metanephrines and vanillylmandelic acid and blood catecholamine levels were estimated in 2 cases. CT scan and/or MRI were used in the imaging of all cases. 123I-MIBG was used in only 1 patient. All patients underwent surgical treatment.

Results: The definitive diagnosis was made by histopathological examination of the removed tumors and was confirmed in all cases by the immunohistochemical stains of chromogranin A and S100 protein. Follow-up ranged from 2 to 70 months (mean = 29.75 +/- 33.2). There was no recurrence or metastasis in any case following surgery.

Conclusion: Pre-operative diagnosis of nonfunctioning paraganglioma is difficult, but the tumors should be suspected in patients who have hypertension, hematuria or mass effects due to the tumor growth in the pelvis and/or retroperitoneum. Resection is the treatment of choice with no recurrences noted.

9 PRIMARY GASTRIC LYMPHOMA : A CLINICOPATHOLOGIC STUDY

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Background/Aims: This study aims to define the clinicopathologic criteria of primary gastric lymphoma in view of MALT concept and to present the outcome after different treatment modalities.

Methodology: 52 cases of primary gastric lymphoma treated between Jan.1990 and Dec.2003 were reviewed. All tissue specimens (endoscopic or surgically resected) were re-examined. Tumors were staged according to Ann Arbor staging system and the Musshoff modification (IE in 30.3%, IIE in 39.4% and IIIE in 30.3%). Forty-seven patients underwent gastrectomy with postoperative chemotherapy for 31 patients. Five patients were treated by chemotherapy only.

Results: Primary gastric lymphoma represented 71.2% of cases of gastrointestinal lymphoma and 11.2% of all gastric malignancy. The mean age was 48 years and male to female ratio was 2.5:1. Epigastric pain was the commonest symptom (in 89%). Ulcer-like lesions were the commonest (60.3%) and the most commonly involved site was the lower third (43%). The respectability rate was 89 %. The mean overall survival was 9.6 years survival was 10.2 years after gastrectomy, 8.3 years after gastrectomy with chemotherapy and 5.6 years after chemotherapy. (p=0.0067).

Conclusions: Primary gastric lymphoma is not an uncommon tumor. Gastritis-like lesions are rare. If the tumor is resectable, gastrectomy will provide the most accurate means of diagnosis, staging and locoregional control of the disease.

10 ADJUVANT CHEMORADIOTHERAPY, WITH 3-DIMENSIONAL CONFORMAL IRRADIATION COMBINED WITH CAPECITABINE (XELODA®) AS RADIOSENSITIZER FOR GASTRIC CANCER

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Introduction: Gastric adenocarcinoma still has a poor prognosis, with high rate of locoregional tumor recurrence even after curative surgery, while there are controversial results regarding the potential additional benefit of adjuvant therapies.

Methods: The preliminary results of the adjuvant chemoradiotherapy (CRT) with a 3 dimensional conformal radiation (3DCRT) in combination with capecitabine (Xeloda®) oral use as radiosensitizer in two males, 54 and 68 years, with moderate and poor differentiated gastric adenocarcinoma are presented. Both patients underwent gastrectomy and pathological TNM-classification after surgery was pT3N2M0 and pT3N3M0. In order to improve the local control, it was decided to further treat the patients with adjuvant CRT. 3DCRT was administered using a linear accelerator of 18MEV. Initially the patients underwent a CT simulation of the radiation field and a total number of about 50-55 slices were sent to EXOMIO 3-DCT simulation system (Medintec, Bochum, Germany). All countered slices were sent to treatment planning system PLATO for the dosimetric calculations required from the 3DCRT. All beam characteristics were delivered to the linear accelerator, through the information and verification system LANTIS. A total dose of 4500cGy in 25 fractions, 180cGy/fraction was administered. During radiotherapy, they were concurrently received capecitabine 500mg peros, 3X2/daily, after laboratory examinations, which were normal. After the completion of radiotherapy, the capecitabine oral use was continued, in a dose of 1250mg/m² twice daily for 3 weeks every 4 weeks.

Results: During the follow-up, twelve months after radiotherapy, both patients had stable disease, without evidence of locoregional progression or distal metastases. No severe toxicity was observed due to CRT, which was completed without complications. Except for mild diarrhea without clinical significance, no other severe side effects were reported.

Conclusion: Although great number of patients is needed, we consider the adjuvant CRT, especially the combination of 3DCRT with capecitabine orally as radiosensitizer, after optimal surgery, safe and potentially effective treatment for gastric cancer.

11 THE PATTERNS OF CLINICOPATHOLOGICAL FEATURES, MANAGEMENT, AND SURVIVAL OF A GASTRIC ADENOCARCINOMA IN THE SULTANATE OF OMAN

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Background: Gastric carcinoma (GC) is the second most frequent cancer worldwide and the most common cancer in the Sultanate of Oman. Ethnic differences in clinicopathological features and survival are observed with variation in surgical and medical management. The aim is to study the clinicopathological features, management, and survival trends of gastric cancer in Oman.

Methods: 339 gastric adenocarcinoma cases diagnosed and treated at three main hospitals in Oman over 11 years were analyzed in two periods 1993-1998 (period I), and 1999-2004 (period II).

Results: 339 patients were included (221 males, 118 females). In both periods GC was disease of elderly males. Antral (64.7% vs 57.7%) ulcerating (79% vs 70%) intestinal (88.5 vs 87.9%) GCs predominated in the two periods with no significant differences. The main histopathology was adenocarcinoma with slight increase of signet cell variant (7% to 20%, $P=0.03$) in period II. Advanced stages III and IV constituted 71% and 76% of all patients for period I and II respectively ($p=0.9$). More D2 lymph node dissections, and increase use of adjuvant chemo-radiotherapy and palliative chemotherapy were noted in period II. The median survival for the entire cohort was 12 months (95% CI 9.7-14.4) with 5 year overall survival rate 15.6%. The 5-year overall survival for first and second periods was 14% and 17% ($p=0.5$) respectively.

Conclusion: GC in Oman is disease of males which is predominately distal, intestinal, and ulcerative. It continues to present in advanced stages and despite the more aggressive surgical and medical treatment trends there is no improvement in survival which underscore the need for early diagnosis to achieve a better outcome.

12 LOCAL RESECTION AS AN ALTERNATIVE OPTION IN THE MANAGEMENT OF AMPULLARY CANCER.

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Background and aims: To report the results of the management of tumors of the ampulla of Vater by local resection.

Patients & Methods: From 1990 to 2000 a total of 32 patients underwent operation for ampullary cancer. Twenty-one of them underwent pancreaticoduodenectomy and 9 local resection of the ampullary lesion. The remaining 2 patients underwent palliative surgery. Pancreaticoduodenectomy was the first choice as the type of surgical treatment. Local resection was the preferable treatment when the ampullary lesion was less than 2cm in diameter, the pre-operative biopsy showed a pT1 cancer or adenoma of the ampulla of Vater and/or the patient's concomitant medical illness or age contraindicated a major operation such as Whipple's procedure.

Results: When the final histological diagnosis was compared with the preoperative histological finding on biopsy, accurate diagnosis was preoperatively established in 24 patients. The hospital morbidity was 18.7% (9 complications in 6 patients). All the complications occurred in patients who underwent pancreaticoduodenectomy. Following local excision of the ampullary cancer, the survival rate at 3 and 5 years was 77.7% and 33.3% respectively. Among the patients that underwent Whipple's procedure, the 3-year survival rate was 76.2% and the 5-year survival rate 62%.

Conclusions: In this series, local resection was a safe option in patients with significant co-morbidity or small ampullary tumors (<2cm), and was associated with satisfactory long-term survival rates.

13 EVALUATION OF TARGETED THERAPY CHALLENGES IN HEPATOCELLULAR CARCINOMA: IMMUNOHISTOCHEMICAL EXPRESSION OF EGFR CORRELATING WITH MOLECULAR DETECTION OF THE SPECIFIC GENE ALTERATIONS AND CHROMOSOME 7 INSTABILITY IN INTRAOPERATIVE IMPRINTS AND SURGICAL SPECIMENS USING TISSUE MICROARRAYS

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Background: EGFR over activation appears to be a very important genetic event in tumor growth and progression. EGFR gene is located at chromosome 7p12 and the main mechanisms of molecular deregulation include amplification, deletion or point mutations. Molecular targeting strategies for cancer therapy include EGFR inhibition via extracellular domain monoclonal antibodies such as cetuximab and intracellular receptor catalytic domain small molecule tyrosinase kinase inhibitors such as gefitinib and erlotinib. Although EGFR immunohistochemical expression is observed in many cancers only a small proportion is appropriate for target therapy response.

Methods: Using Tissue Microarray Technology 20 hepatocellular carcinomas firstly diagnosed by intraoperative imprints cytology (7 High, 8 Moderate and 5 Low differentiated) and 5 cases of cirrhotic liver were obtained and embedded into one paraffin block (2 spots of each case with a core diameter of 1mm). Immunohistochemical stain for anti-EGFR extracellular domain monoclonal antibody combined with Chromogenic In Situ Hybridization (CISH-Zymed Corp) for the detection of chromosome 7 instability and specific gene status were performed in 2 and 5 μ m sections and in intraoperative imprints. Finally using a semi-automated Image Analysis System we evaluated the immunohistochemical stain optical density and the number of signals of chromosome 7 centromeres and gene copies per nucleus. Statistical analysis was performed by SPSS version 11.0 software.

Results: A significant proportion of the tumors showed over expression of the protein 12/20 (60%) and CISH application showed low level EGFR amplification in cell sub populations of 2/12 (16%) cases. Co-evaluating chromosome 7 instability with amplification we observed that these 2 cases were correlated with low differentiation and staging ($p < 0,001$). But over expression was not correlated with 3+ qualitative evaluation of immunohistochemical stain.

Conclusions: The results indicate that accurate detection of EGFR amplification is a critical process because this genetic event correlates with biological behavior in hepatocellular carcinoma. Although the main mechanism of over expression seems to be not the gene amplification but point mutations of intracellular cytoplasmic tyrosine kinase domain or reduced expression of EGFR RP (related protein-negative feedback system), a sub group of cases possibly offers the appropriate molecular substrate for application of targeted monoclonal antibody therapy. Also intraoperative imprints afford better cytological details and sampling capability than frozen sections because of the tumor architecture and nuclear preservation.

14 IMAGE-GUIDED TOMOTHERAPEUTIC INTENSITY-MODULATED RADIATION THERAPY (IG-IMRT) FOR HEPATOCELLULAR CARCINOMA

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Despite evidence for hepatocellular carcinoma (HCC) tumor response to radiation therapy, the limited radiation tolerance of the adjacent normal liver has prohibited wider use of this treatment modality in this disease. Recent developments in radiation therapy such as intensity-modulated radiation therapy (IMRT), image-guidance, and stereotactic body radiation therapy (SBRT) hold the potential to improve radiation treatments by increasing conformal dose planning and delivery enabling superior normal tissue sparing.

Between 11/00 and 2/05, 12 patients with HCC were treated by IMRT (Peacock IMRT, Nomos) to mean doses of 64.2 Gy (54-76 Gy). Three patients were treated by SBRT (36 Gy in 3/6 fractions). All patients underwent daily ultrasound-based image-guidance using the BAT device (Nomos). Clinical target volumes averaged 443 cm³ (IMRT: 62-947 cm³; SBRT: 7-86 cm³), with planning target volumes averaging 948 cm³ (IMRT: 221-1857 cm³; SBRT: 36-220 cm³). The radiation exposure to 30% and 50% of normal liver (D30 liver/D50 liver) was kept below 25 Gy and 35 Gy (mean D30 16.0 Gy, mean D50 25.9 Gy), with mean liver doses of 28.7 Gy (25.3-35.7 Gy). In this small series with limited follow-up, no RILD was observed. Thus, we consider these preliminary data encouraging and supportive of future exploration of the technology. The present data document the clinical feasibility of employing the most recent radiation and image-guidance techniques to safely treat HCC. Thus, new consideration for the role and capacity of radiation therapy should be given in the treatment of HCC too large for resection and transplantation. Modern radiation techniques have the capability to offer much more than palliation in the symptomatic near-end situation and should be considered earlier in the disease course than is currently common.

15 QUALITY CONTROL IN RECTAL SURGERY

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Quality control has become very important in the management of rectal cancer. Local recurrence rates vary from 4% to 50% and outcomes differ between surgeons and centers. The department of Surgical Oncology of University Hospital of Crete has developed, in cooperation with the Center for Technological Research (CTR), an electronic database for the patients with rectal and colon cancers. From 1993 to 2004 period 126 patients with rectal cancer have been operated for rectal cancer in our department. Follow-up is complete for 109 patients. All the data was statistically analyzed by CTR. 5% of the patients was stage I, 35% was Stage II, 51% patients was Stage III and 9% Stage IV. 72% of the patients have been treated by LAR, compared with 70% and 69% in the Dutch and the Norwegian Study. The operative mortality was 1, 9%, compared with 2% and 3% in the Dutch and the Norwegian study. 57% of the patients had more than 12 lymph nodes removed. The leakage rate after low anterior resection was 10, 1% which is acceptable, according to the literature. The local recurrence rate was 11, 8%.

The conclusion of this quality control study is that the operative mortality, the leakage rate and the extent of lymphadenectomy are comparable to the relevant literature. The rate of local recurrence after operation for cancer of the rectum can be further decreased by adherence to the technical details of the Total Mesorectal Excision technique and the use of perioperative radiotherapy.

16 COMPARISON OF THE EFFECTS OF THE LOOP COLOSTOMY VERSUS LOOP ILEOSTOMY IN THE PATIENTS AFTER RECTAL CARCINOMA SURGERY

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The aim of this study was to compare loop colostomy (LC) and loop ileostomy (LI) as options for fecal diversion in the patients who underwent elective surgery for mid and low rectal cancer.

Between 2000 and 2004, 74 patients were electively operated for rectal carcinomas with primary colorectal or coloanal anastomosis. There were 34 LC and 40 LI. LC was performed in left epigastrium closer to splenic flexure of transverse colon. The LI was performed at 15-20 cm from the ileocaecal junction. The closure of LC and LI intended to be performed from the local excision.

The formation of LC was significantly shorter than LI (25 ± 3 and 29 ± 4 minutes), ($p=0.001$) respectively. There were no early complications after LC formation, while LI was associated with local skin irritation in 2/40 (5%) and ileus in 3/40 (7,50%) patients. No late complications related to LI were developed, whereas LC was complicated with herniation in 1/34 (2,95%) and prolaps in 3/34 (8,82%) patients. The follow up was available in 32 LC and 38 LI patients. The LC closure was performed in 30 patients and LI closure in 36. The mean time to LC closure was 11 ± 5 weeks and to LI closure 13 ± 5 weeks. The stoma closure rate was 30/34 (88,20%) after LC vs. 36/40 (90,00%) after LI. The reasons for nonclosure was following: for LC recurrence of cancer ($n=1$), and anastomotic problem ($n=1$), for LI reasons were recurrence of cancer ($n=1$), and poor general condition ($n=1$). All stomas were closed from local excision except 3 LI. In these cases adhesiolysis was necessary and stoma closure was conducted from midline access. The time for LC closure was significantly shorter than for LI closure 86 ± 18 min. vs 108 ± 22 min. ($p=0,03$). There was no death related to the closure of LC except for one patient (2,78%) who died from peritonitis developed because of the anastomotic leakage after LI closure. The total secondary morbidity rate was higher after LI closure than after LC: 6/36 (16,67%) vs 1/30 (2,95%). Prolonged ileus 4/36 (11,11%), wound infection 1/36 (2,78%) and anastomotic leakage 1/36 (2,78%) were associated with LI closure while only one prolonged ileus (2,95%) was developed after LC closure.

Loop transverse colostomy seems to be more simple method of proximal fecal diversion associated with less primary and secondary morbidity.

17 NUCLEAR SIZE AS PROGNOSTIC DETERMINANT IN STAGE II AND STAGE III COLORECTAL ADENOCARCINOMA

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Background: We assessed the prognostic value of morphometric nuclear features in Stage II and stage III colorectal cancer (CRC).

Material and Methods: Primary tumors from 123 CRC patients were analyzed using an image overlay drawing system for the following nuclear size features: area, perimeter, diameter, and form features.

Results: The median nuclear area (NA) was 98.8 μm² (range 45.2 μm²–159.4 μm²). NA was not significantly related to age, sex, or tumor grade, but it was larger in stage III disease. NA was significantly different in tumors at different localization (p=0.029). Large NA was significant predictor of recurrent disease (p=0.006). NA was significantly larger in recurrent cases (106.3 μm²) than in non-recurrent ones (96.6 μm²) (p=0.007). NA was a significant predictor of disease-free survival (DFS) in univariate (Kaplan-Meier) analysis (log rank p=0.0239). However lymph node involvement was the most powerful predictor of DFS in multivariate analysis (p=0.024), and disease recurrence the only independent predictor of disease specific survival (DSS).

Conclusions: Quantitative measurement of NA and its value above the median seems to accurately discriminate the patients who are likely to develop disease recurrence among stage II and III colorectal cancer patients. Image morphometry seems to be a useful adjunct tool in examining the subgroup of LN-negative patients to predict the risk of disease recurrence and indications for adjuvant therapy.

Keywords: Nuclear morphometry, nuclear area, colorectal cancer, prognosis, adjuvant therapy.

18 HOW PRACTICE PATTERNS IN RECTAL CANCER PATIENT FOLLOW-UP ARE AFFECTED BY SURGEON AGE

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Background: The follow-up of rectal cancer patients after potentially curative surgery has been shown to vary widely. The optimal schedule for such follow-up remains unknown. This study investigates the relationship between the age of the surgeon and choice of surveillance strategy.

Methods: A questionnaire was sent to one thousand seven hundred and ninety five members of the American Society of Colon and Rectal Surgeons (ASCRS) to measure how these specialists conduct rectal cancer follow-up. Respondents were presented with a scenario in which a rectal cancer patient (TNM stage I-III) had a potentially curative resection. They were asked how often they would use fourteen separate surveillance tests during postoperative years one to five. Repeated measures analysis of variance was used to evaluate if practice patterns were related to the year in which surgeon's formal training was completed, controlling for tumor stage and year post surgery. Participants were also asked which tests they would use to further investigate a postoperative raised serum carcinoembryonic antigen (CEA), and a postoperative chest radiograph showing probable metastatic disease. Chi square analysis was used to compare practice patterns to surgeon age.

Results: Evaluable responses were received from three hundred and forty seven ASCRS members (nineteen percent). Repeated measures analysis of variance revealed no significant relationship between surgeon age and follow-up test ordering schedules. However, follow-up for most modalities was highly correlated with TNM stage and year post surgery, as expected. Though practitioner age was not a factor in the workup of an abnormal postoperative chest radiograph, it was a significant factor in the workup of an elevated postoperative carcinoembryonic antigen test. The diagnostic tests that varied significantly by age were complete blood count, liver function tests, chest radiograph and colonoscopy.

Conclusions: Our study shows that post-operative surveillance practices of surgeons caring for patients with rectal cancer do not vary with practitioner age. We propose that continued medical education (CME) has produced this standardized behavior. However, CME has been less successful in homogenizing other areas of respondent's practice, such as in the workup of a raised postoperative CEA. Therefore we conclude that practitioner age accounts for some of the variation in post-operative management of rectal cancer patients.

19 EFFECTS OF NUTRITIONAL SUPPORT IN PATIENTS WITH COLORECTAL CANCER DURING CHEMOTHERAPY

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Background: Cancer cachexia occur in significant number of patients (pts) with cancer. Benefit of nutrition support still remains unclear.

Rationale: To examine does nutritional support (counseling, oral liquids, megestrol acetate) has influence on nutritional status and symptoms prevalence in patients with colorectal cancer during chemotherapy.

Methods: We retrospectively (group A) examined data of 173 pts who were treated in 3 years period without nutritional counseling. Prospectively (group B-215) pts, we offered to our pts individualised nutritional counseling, liquid supplementation, and megestrol acetate. Dietary intake (Nottingham Screening Tool Score) and body weight (Body Mass Index) were monitored before, during and after chemotherapy. The nutritional plan was modified when necessary.

Results: During 6 years period we were treating 388 pts with colorectal cancer. Baseline, in both groups about 55% of pts were moderately or severe malnourished. In group A during chemotherapy 140 (80.9%) of pts decreased in weight gaine 2-5 kg and 77 (44.5%) were severe malnourished on the end of chemotherapy. In group B, 184 (85.6%) of pts gain weight. The effect of nutritional support was most expressed in the group receiving megestrol acetate and nutritional counseling after 4 weeks of therapy. Average weigh gaine was 1.5 kg (0.6-2.8).

Conclusion: With nutritional support our pts with colorectal cancer gain weight and had better Quality of Life during chemotherapy.

20 DOES IRINOTECAN INDUCE RESECTABILITY OF LIVER METASTASES FROM COLORECTAL CARCINOMA?

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Objective: In patients with liver metastases (LM) from colorectal carcinoma, liver resection offers the chance of long-term survival. However, resectability rate is only 10-25% due to multiple bilobar LM or infiltration of main hepatic/portal vein branches. Modern neoadjuvant chemotherapy has the potential ability to render formerly unresectable patients resectable. Aim of the present study is to assess influence of chemotherapy with irinotecan-based regimen on resectability rate of LM in patients with colorectal carcinoma.

Patients and Methods: Between January and December 2004, 60 patients with metastatic colorectal carcinoma were treated with the CLF1 regimen (irinotecan 180 mg/m² day 1; 5-Fu 400 mg/m² day 1 and 600 mg/m² day 1, 48 hours infusion; leucovorin 200mg/m² days 1 and 2) every two weeks. In 29 out of the 60 patients (48%), liver was the only metastatic site of the disease.

Results: Eleven patients were scheduled for primary surgical exploration. In 4 patients understaging of the disease in the preoperative work-up was found and further resection was postponed. In 7 patients following resection procedures were performed (7/11; resectability: 64%): hemihepatectomy – 3 (1 extended right-, 1 right- and 1 left- hemihepatectomy), bisegmentectomy – 3 (in 1 patient bilobar lesions), (mono)segmentectomy – 1. None of the four initially explored patients did have a response justifying re-exploration and resection, after subsequent chemotherapy with CLF1. Whereas out of 18 patients with primary non-resectable LM, three patients were subsequently explored due to partial response to the chemotherapy. Resection of LM was done in 1 out of the 3 patients. Altogether, resectability rate of primary non-resectable tumours following CLF1 chemotherapy was 14% (1/7), and it tended to be lower as compared to primary non-treated LM (p=0.066; Fisher exact test).

Conclusions: Irinotecan-based chemotherapy in patients with initially non-resectable LM from colorectal carcinoma renders limited resectability.

21 CLINICAL SIGNIFICANCE OF CHROMOSOME 8 IMBALANCES IN PRIMARY COLORECTAL CARCINOMAS: A FISH STUDY WITH DNA PROBES FOR 8P22, 8CEN AND 8Q24 IN PARAFFIN-EMBEDDED TUMOUR SECTIONS

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In a series of 150 primary colorectal carcinomas cytogenetically investigated at surgery, cytogenetic features were correlated with patient survival by univariate and multivariate analyses, using classical clinicopathologic parameters as covariates. Several cytogenetic tumor features were found to be valuable predictors of prognosis. Among them, structural aberrations of chromosome 8 were significantly associated with shorter survival, independently of all other chromosome changes in the tumour genomic profile. Furthermore, in the subset of patients with stage III carcinomas, the presence of chromosome 8 rearrangements was a stronger predictor of prognosis than any other parameter, including stage and tumor grade. To evaluate whether a fluorescence in situ hybridization (FISH) test can be used as part of a routine prognostication system in colorectal cancer, we have applied interphase FISH with DNA probes specific for 8p22 (lipoprotein lipase gene/spectrum orange), centromere 8 (8cen/spectrum aqua), and 8q24 (c-myc gene/spectrum red) in paraffin-embedded tumour sections from colorectal carcinomas with karyotypically documented chromosome 8 alterations. The results of FISH analysis in 11 investigated histological sections confirmed the occurrence of 8p22 loss and 8q24 gain in all samples. The average percentage of nuclei with loss of 8p22 was 71,5% (range, 56%-81%) whereas the average percentage of nuclei displaying gain of 8q24 was 21,7% (range, 3%-40%). These findings demonstrate that FISH analysis could unfailingly detect imbalances of chromosome 8 in histological sections of colorectal carcinomas, without requirement of fresh tumour samples, culturing tumour cells and performing complete karyotypic analysis. Since changes of chromosome 8 are associated with a highly metastatic tumour potential and poor disease outcome, their detection by a simple and reliable FISH test could assist oncologists in deciding which patients might benefit from adjuvant treatment after surgery, even in the absence of apparent lymph node metastases.

22 EPIDURAL ANALGESIA FOR PATIENTS SUBJECTED TO COLORECTAL CANCER SURGERY. COMPARATIVE STUDY OF TWO ADMINISTRATION TECHNIQUES

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Objective: The ideal perioperative analgesia should provide effective pain relief, avoid the detrimental effects of the stress response, be simple to administer without the need for intensive monitoring and have a low risk of complications. The aim of our study is to compare two administration techniques for perioperative epidural analgesia in colorectal cancer surgery.

Materials and Methods: Our study included 32 patients with primary colorectal cancer subjected to elective open colorectal surgery. All our patients received postoperative epidural analgesia until day 4 from a catheter positioned in the L3-L4 interspace and they were divided in two study groups, group M who received postoperative analgesia in the form of bolus infusions of Fentanyl added to 0.2% Ropivacaine every 12 hours from the epidural catheter while group F received Fentanyl 3mcg/ml in 0.2% Ropivacaine with a continuous infusion pump (PCEA). Doses were titrated according to age in both groups. Pain intensity was tested three times daily using a visual analog scale (0-100). Rescue analgesia in the form of Lornoxicam 8mg was administered at VAS score exceeding 40. Postoperative evaluation included mental status, cardiorespiratory and gastrointestinal functions, motor and sensory blockage assessments.

Results: Pain scores were <38 (SD±2) in both groups. Patients in the M group showed better cardiocirculatory stability and none patient from either group manifested motor or sensory block. No differences were observed between groups in time to oral intake patient ambulation, return of bowel function or length of stay.

Conclusions: Both analgesic techniques were associated with satisfactory postoperative pain control. Optimal pain management decreases the stress response to surgery, reduces complications, improves recovery times and results in improved economic and quality-of-life outcomes.

23 THE CHANGES OF THE ENDOGENOUS DIAZEPAM CONCENTRATION IN THE SERUM AND THE RISK OF DEVELOPING NEOPLASTIC METASTASES IN THE LIVER

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Purpose of the study: The aim of the research was to determine the changes of the endogenous diazepam concentration in the serum (DCS) of patients radically treated because of breast cancer, large bowel cancer and stomach cancer, in the period preceding the neoplastic metastases (NM) to the liver.

Material and method: The analysis included 64 patients (30 men and 34 women) aged 45 to 74 years, radically operated because of breast, large bowel and of stomach cancers. All the patients were included in a similar model of postoperative controls, in which, among others, was the DCS estimation. During the study the patients were prohibited to take any medicines of the benzodiazepines group, this implied that in the end, there were 64 persons in the group analysed. In the course of the post-operative controls (the longest observation period lasted 5 years) metastases to the liver occurred in 18 patients in a period of 6 months to 4 years after radical treatment.

Results and conclusions: 1. The DCS was within the range of the reference values of this benzodiazepine in 92.2% patients studied, after three months following the end of the radical treatment of the neoplastic disease.

2. In the course of the observation conducted, the DCS was noted in 23.4% of those analysed, and in this group up to 86.6% patients developed NM in the liver in the later period.

3. The increase of the DCS preceded the appearance of the NM in the liver by three months to one year.

4. The average DCS in the period preceding the occurrence of NM in the liver was 11 times higher than the average reference values of this benzodiazepine.

5. The post-operative monitoring of the endogenous DCS may be a valuable criterion to select the patients threatened with a high risk of developing NM in the liver.

24 INTRAHEPATIC RECURRENCE OF HEPATOCELLULAR CARCINOMA TREATED BY PERCUTANEOUS ETHANOL INJECTION. COMPARISON BETWEEN VIRUS C AND B LIVER CIRRHOSIS.

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Percutaneous ethanol injection (PEI) is now widely used for the treatment of hepatocellular carcinoma (HCC) in patients with liver cirrhosis because of its feasibility and relative safety for patients with deteriorating liver function. However, recurrence rates after PEI or resection remain high with most of the recurrence in the remnant liver.

Aim: to study the intrahepatic recurrence rate after PEI in respect to different etiologies of viral liver cirrhosis in a Romanian population.

Methods: 60 patients with viral liver cirrhosis (virus C 40 pts, virus B 20 pts) and HCC (1-2 lesions, mean size 28mm, range 15-46 mm) were treated by PEI between 1998-2003. The patients were followed up for 6-36 months (mean 24 months). The recurrence rates and types (local or distant) were noted at 6,12 and 24 months.

Results: In respect to the etiology of cirrhosis the recurrence rates at 6,12 and 18 months were 40%, 75% and 80% for virus C and 0%, 10% and 20% for virus B cirrhosis. Local recurrence rates at 6,12,18 months were 20%, 25% and 25% in virus C cirrhosis group and 0%, 0% and 0% in virus B group. The distant recurrence rates were 20%, 50% and 55% for virus C and 0%, 10% and 20% for virus B cirrhosis. The distant recurrences were 100% of nodular type for virus B cirrhosis. In virus C cirrhosis the distant recurrences were plurifocal in 76.9% of patients and nodular in 23.1%.

Conclusions: The recurrence rates after PEI are higher in HCC and virus C cirrhosis in comparison with virus B cirrhosis for both local and distant recurrences. The distant recurrences are plurifocal in most of the patients with HCC and virus C cirrhosis.

25 IMAGE-GUIDED TOMOTHERAPEUTIC INTENSITY-MODULATED RADIATION THERAPY (IG-IMRT) FOR GALLBLADDER CANCER

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Purpose: Analysis of technical parameters and preliminary outcomes of patients treated by IG-IMRT for gallbladder cancer.

Methods: Between 8/2001 and 2/2005, ten patients with gallbladder cancer were treated with IMRT to median doses of 60 Gy (range 54 to 70 Gy) prescribed as the minimum dose received by the PTV. Daily ultrasound-based image-guidance was used to optimize patient and PTV setup. We recorded shift data for spatial positioning analysis, as well as preliminary toxicity and survival data. To assess the impact of improved patient positioning and corresponding reduced safety margins (range 6 to 15 mm), the actual delivered dosimetry was compared with plan simulations with more conventional PTV margins of 20 mm.

Results: In 224 recorded image-guidance attempts, mean absolute corrective shifts from skin mark position were 5.6 ± 4.8 , 8.6 ± 5.5 , and 8.0 ± 9.2 mm along the x, y, and z axis, respectively. Shifts along one axis >10 , >15 , and >20 mm were observed in 55%, 28%, and 17% of alignments. The mean magnitude vector of correction was 14.8 ± 9.6 mm, with 63%, 36%, and 20% of alignments corrected for a magnitude vector of >10 , >15 , and >20 mm, respectively. Clinically, treatment was well tolerated, with one patient reporting RTOG grade 3 acute radiation morbidity. All other patients exhibited Grade 2 or lower acute toxicity, with 5/10 reporting no morbidity greater than grade 1. At the time of analysis, 6 patients were living, with 4 deceased. Preliminary one-year actuarial survival was 63% (5/8 with actual 12 months follow-up). Median overall survival was 16.5 months from initiation of therapy (range 2-28 months). Treatment plan comparison revealed that daily image-guidance enabled a statistically significant average PTV reduction of 46% (mean volumetric difference between delivered and re-computed PTV was 642 cm^3).

Conclusion: IG-IMRT is a feasible mechanism of delivering conformal radiation doses to tumors of the gallbladder. In our limited clinical experience, moderate dose escalation in conjunction with tighter safety margins resulted in acceptable acute toxicities and encouraging survival data.

26 CHEMOTHERAPY IN PATIENTS WITH NONRESECTABLE CANCER OF THE BILIARY SYSTEM OR ADVANCED GALLBLADDER CANCER: DO ELDERLY HAVE BENEFIT AT ALL?

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Introduction: Adenocarcinomas of the bile ducts (BSCa) and gallbladder (GBCa) are highly malignant neoplasms with a very poor prognosis. Chemotherapy (cht) plays only a palliative role and responses are transient without prolonged survival.

Aim of the study: to evaluate effectiveness of gemcitabine(G) and cisplatin(CP) combination protocol in achieving Clinical Benefit Response(CBR) for patients(pts) with nonresectable BSCa and with advanced GBCa and to evaluate the differences between younger and elderly pts. For this type of tumors we took 60 years as borderline for elderly.

Results: during five years period we cured 38 pts with BSCa and GBCa with mean age of 52.4 ± 4.8 years. There was 23 females with mean age of 50.2 ± 3.8 years, and 15 men with mean age 53.7 ± 4.3 years. In the group of elderly there was 9 females with mean age of 61.8 ± 2.9 years, and 6 men with mean age of 62.4 ± 2.9 years. 25 pts (65.8%) had locally advanced disease and 13 pts (34.2%) metastatic disease. Pts achieved G 1000 mg/m² intravenous once per week for seven times. CP 100 mg/m² iv was administered at day 1, 15, 29 and 43. Number of applied cycles was 1-10 (median 4 cycles). Partial response rate achieved 22 pts-57.9%. 36 pts-94.7% achieved CBR. Pain measured at VAS scale before cht was 5,1; and after 1st cht cycle 2,1. Karnofsky Performance Status before cht was 62.4%, and after 1st cycle 78.8%. Median duration Clinical Benefit was 21 weeks. 29 pts (76.3%) developed fatigue gradus II-III (WHO); 20 pts (52.6%) expressed nausea gradus II (WHO); elderly had stronger fatigue (gradus III) versus younger; also as more serious leucopenia and trombocitopenia (gradus III) than younger (gradus II).

Conclusions: There was no difference between younger and elderly pts in number of applied cycles; also no difference in achieving partial response rate and CBR. There was difference in developing side effects; elderly had more serious fatigue, leucopenia and trombocitopenia than younger. This results indicate that the treatment of GBCa and BSCa with gemcitabine and cisplatin is effective and well tolerated also to elderly pts and leads to Clinical Benefit for both groups. The role of cht in this malignancies is palliation and achieving better Quality of Life more than prolonging survival time.

27 MESSAGE-ADJUSTED NETWORKS IN GASTRO-ENTERO-PANCREATIC (GEP) ENDOCRINE SYSTEM

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Intercellular communication is an essential issue for continuity of life in multicellular organisms. Several types of communication such as autocrine, paracrine, juxtacrine, endocrine, neurocrine and lumencrine coordinate body functions to maintain homeostasis. In this study, we established some intercellular network models to understand the physiology of GEP endocrine system based up-to-date information from medical publications. Major key words were modes of regulations mentioned above, GEP cells, hormones, peptides and neuro-transmitters. We propose that if we orientate to a transmission of a unique message we could design message-adjusted networks (MAN) between cells. Designing MAN in neuro-endocrine physiology could help to explain complex physiologic events and physiopathology of some diseases such as anorexia, obesity, irritable colon syndrome, inflammatory bowel diseases and neuroendocrine tumours, as well as to generate new treatment concepts. Finally, we estimate that clarifying chemical communication systems in the human body could be a novel project after human genome (HUGO) and protein organisations (HUPO).

28 CHEMOTHERAPY WITH TS-1 FOR POSTOPERATIVE PATIENTS AFTER RESECTION FOR GASTRIC CARCINOMA

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Background: TS-1 is an anticancer drug composed of Tegafur, Gimestat, and Otastat potassium. The response rate of TS-1 for advanced gastric cancer in the late Phase II trial was 46.5%. We have reported that the overall response rate was 37.5% in our series of patients with advanced or recurrent gastric carcinoma.

However, when administered for postoperative patients by the conventional regimen, adverse effects occurred frequently. Therefore, we have modified the conventional regimen and compared the frequencies of adverse effects among the conventional and modified regimens.

Patients and Methods: Thirty-nine patients who received two or more courses of chemotherapy with TS-1 after resection for gastric carcinoma were included in the study. Twenty patients received TS-1 for adjuvant therapy after curative resection, and 13 patients for recurrent disease. Six patients received TS-1 after non-curative resection. The patients were divided into the three groups. Group A (conventional regimen): 17 patients who received 80 mg/m²/day of TS-1 for 28 days followed by 14 days rest. Group B: 16 patients who received 60 mg/m²/day of TS-1 for 28 days followed by 14 days rest. Group C: 6 patients who received 80 mg/m²/day of TS-1 for 21 days followed by 14 days rest. The mean number of courses performed was 5.8, 3.3 and 5.0, respectively in groups A, B and C. The frequencies of adverse effects in patients in the three groups were compared. The survival of patients with adjuvant therapy was analysed.

Results: Adverse effects occurred in 100%, 81% and 67%, respectively, of the patients in groups A, B and C. Adverse effects of grade 3 or more occurred only in patients in group A (24%). Forty-one percent and 6%, respectively, of the patients in groups A and B, required dose reduction. There have been no differences in survival of patients with adjuvant therapy between the three groups.

Conclusions: In chemotherapy with TS-1 for postoperative patients, modified regimens would be safer and tolerable.

29 IMAGE-GUIDED TOMOTHERAPEUTIC INTENSITY-MODULATED RADIATION THERAPY (IG-IMRT) FOR PANCREATIC CANCER

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Purpose: Analysis of clinical and technical parameters for a series of patients treated with image-guided sequential tomotherapeutic intensity-modulated radiation therapy (IMRT) for pancreatic cancer.

Methods and Materials: Between 11/00 and 11/04, 34 patients with pancreatic cancer were treated with IMRT to median doses of 60 Gy (range 46.8 to 66 Gy) prescribed as the minimum dose received by the PTV (planning target volume). Concomitant chemotherapy (5FU, Xeloda, CPT11, or gemcitabine) was administered in 74% of cases. Daily ultrasound-based image-guidance was used to optimize patient and target setup. We recorded corrective shift data for spatial positioning analysis, as well as preliminary toxicity and survival data.

Results: In 1344 recorded patient image-guidance attempts, mean absolute corrective shifts from skin mark position were 3.6 mm (range 1.4-7.3 mm), 4.9 mm (11-12.7 mm), and 3.3 mm (0.9-11.3 mm) along the x, y, and z axis, respectively. Shifts in one principal direction >10, >15 and >20 mm were observed in 21%, 3%, and 1% of alignments. The mean magnitude vector of positional correction was 8.3 mm (3.3-23 mm). Treatment was stopped at mean doses of 53 Gy (range 46.8-54 Gy) in 4 patients due to RTOG grade 3 acute radiation morbidity and chemotherapy associated hand-foot syndrome. All other patients exhibited Grade 2 or lower acute toxicity, with 10/34 reporting no morbidity greater Grade 1. At the time of analysis, 17/34 patients were alive with a median clinical follow-up of 12 months.

Conclusion: Ultrasound-based image-guided IMRT is a feasible mechanism of delivering conformal radiation doses to tumors of the pancreas. In our limited clinical experience, moderate dose escalation in conjunction with tighter safety margins enabled by daily image-guidance resulted in acceptable acute toxicities and encouraging preliminary survival data. This treatment approach may ultimately result in improved local tumor control and allow for further radiation dose escalation and/or chemotherapy intensification.

30 POSSIBLE ROLES OF RAGE AND MMP-9 FOR THE INVASIVE ABILITY IN HUMAN PANCREATIC AND BILIARY TRACT CARCINOMA CELLS

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Objective: Amphoterin is considered as a regulator for the ability of invasion and migration in tumor cells and embryonic neurons through binding to receptor for advanced glycation end products (RAGE), that is an important molecule for invasion. As matrix metalloproteinases-9 (MMP-9) has been reported to play a critical role in tumor progression and metastasis, we have examined the relation of RAGE and MMP in human pancreatic and biliary tract carcinoma cells.

Methods: To see the involvement of RAGE, three representative human pancreatic carcinoma cells which show different metastatic potential (PANC-1 and MIA PaCa-2 as the cells with high ability, BxPC-3 as with low) and human biliary tract carcinoma cells (SK-ChA-1, TGBC-1 and NOZC-1) were rendered for the study. The expression of RAGE was examined by Western blotting and RT-PCR and that of MMP-9 protein was examined by Western blotting. Cell invasion ability was determined using Matrigel invasion assay.

Results: RAGE was strongly expressed in high metastatic cells of MIA PaCa-2 and PANC-1 and was little in BxPC-3 that has low ability. Similarly, expression of MMP-9 showed almost same tendency. Meanwhile, RAGE was strongly expressed in SK-ChA-1 and NOZC-1 that have high invasion ability based on the cell invasion assay through Matrigel. On the contrary, RAGE was faintly expressed in TGBC-1 that has low ability.

Conclusions: RAGE and MMP-9 are expressed in concordant to the metastatic ability of the human pancreatic and biliary carcinoma cells. Control of these molecules might be a key to regulate the metastatic ability of these cancers and this may be exploited in targeted therapy of the cancer.

31 SWEET'S SYNDROME ASSOCIATED WITH PANCREATIC CANCER: ABOUT 3 CASES

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Background and Objective: During the last years, several cases of various neutrophilic dermatosis, mainly Sweet's syndrome cases, have been reported in association with myelodysplastic syndromes, myeloid hematopoietic disorders and solid tumors (Wallach D. *Rev Med Interne* 2004). We report three original new cases of neutrophilic dermatosis associated with pancreatic cancer.

Patients: The first case concerns a 32 year-old patient, which was admitted to our hospital for recent weight loss (>10 kg) and high fever (>39°C). The physical examination revealed the presence of inflammatory cutaneous lesions in the thigh region and a swollen Troisier's node. There was in addition an important inflammatory syndrome (CRP >150 mg/l) and an increased WBC count with a left shift (neutrophil count >30 10⁹/l). The histological evaluation of these cutaneous lesions demonstrated a neutrophilic dermatosis process, whereas the histological evaluation of the lymph node demonstrated a pancreatic adenocarcinoma. The second case concerns a 19 year-old young woman presenting a metastatic pancreatic adenocarcinoma, which was made stable 3 months before her admission, under chemotherapy with CDDP and 5FU in association with G-CSF. This patient abruptly presented a febrile syndrome, an increased WBC count with a left shift (neutrophil count >20 10⁹/l) and a Sweet syndrome, typically revealing a flare-up of their disease. The cutaneous lesions were treated by corticoids; the carcinoma was treated by gemcitabine. The third case concerns a 65 year-old patient who was admitted to our clinic for long-standing fever (>38°C). The clinical examination revealed the presence of inflammatory nodular lesions in the thigh area giving evidence to a nodular erythema. Biologically, it existed an inflammatory syndrome (CRP >100 mg/l) and a leucocytosis (WBC >18 10⁹/l). The histological examination of the cutaneous lesions revealed a neutrophilic dermatosis. The rest of the patient evaluation demonstrated a pancreatic cancer with hepatic metastases. This patient died soon, abruptly.

Conclusions: All the present observations illustrate the paraneoplastic character of certain neutrophilic dermatoses, which, in the above three cases, were either associated or revealing the metastatic pancreatic cancer. The presence of fever and an important inflammatory syndrome accompanied by a leucocytosis in all these observations could raise an investigation for the potential role of certain cytokines in the pathogenicity of the whole process (as seen in the second case).

32 CO-TARGETING EGFR AND C KIT PROTEIN IN DUCTAL PANCREATIC ADENOCARCINOMA: IMMUNOHISTOCHEMICAL AND MOLECULAR STUDY USING TISSUE MICROARRAYS AND COMPUTERIZED IMAGE ANALYSIS

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Background: Biologic significance of c kit protein and EGFR over expression in pancreatic cancer is unclear. EGFR gene is located at chromosome 7p12 and c kit at 4q11-12. The main mechanisms of molecular deregulation include amplification, deletion or point mutations. Molecular targeting strategies for cancer therapy include EGFR inhibition via extracellular domain monoclonal antibodies such as cetuximab and intracellular receptor catalytic domain small molecule tyrosinase kinase inhibitors such as gefitinib and erlotinib. Respectively Glivec (Imatinib) is one of the first targeted oncology drugs which acts as signal transduction inhibitor targeting c kit protein.

Methods: Using Tissue Microarray Technology, 50 ductal pancreatic adenocarcinomas (10 High, 20 Moderate and 20 Low differentiated) were obtained and embedded into one paraffin block with a core diameter of 1mm. Immunohistochemical stain for anti-EGFR and anti CD 117 combined with Chromogenic In Situ Hybridization (CISH-Zymed Corp) for the detection of chromosome 7 instability and specific EGFR gene status were performed in 2 and 5 µm sections respectively and using intraoperative imprints and ThinPrep cytological specimens. Finally using a semi-automated Image Analysis System we evaluated the immunohistochemical stain optical density and the number of signals of chromosome 7 centromeres and gene copies per nucleus. Statistical analysis was performed by SPSS version 11.0 software.

Results: A significant proportion of the tumors showed over expression of EGFR 19/50 (38%). C kit over expression was observed in 12/50 (24%). CISH showed low level EGFR amplification in cell sub populations of 2/19 (11%) and deletion in 4/19 (21%) cases. Co-evaluating EGFR and c kit immunohistochemical stain we find a co-over expression in 6/50 (12%) but this event was not correlated with any clinicopathological factors of the tumor (p>0,05).

Conclusions: The results indicate that although the main mechanism of over expression seem to be not the gene amplification for EGFR gene, a sub group of cases which also over express c kit possibly offers the appropriate molecular substrate for combined targeted therapy.

33 ANTISENSE CHEMORADIOIMMUNOTHERAPY CONSISTING OF ANTI-CASM SCFV LINKED ONTO HIGH-ENERGY RADIOISOTOPES, VINOIRELBINE-TARTRATE AND 21-NUCLEOTIDE DOUBLE-STRANDED SIRNA TARGETED TO DNMT1 INDUCE TYPE I AND TYPE II PCD IN PANCREATIC AND PERIAMPULLARY CA CHARACTERISED BY HYPERMETHYLATED ONCOSUPPRESSOR GENES RASSF1A, RAR-B2, BRCA1, DUSP6/MKP-3 AND OVEREXPRESSION OF ONCOGENES BCL-2, CASM, CDC25C AND RAF-1.

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Introduction: Very little is known about the etiology of pancreatic Ca the most lethal of the major malignancies. The primary therapy of unresectable pancreatic Ca consists of combined radiation and chemotherapy. However, pancreatic Ca is resistant to almost all cytotoxic drugs and radiation making it one of the most aggressive malignancies in human with the worst mortality. The failure of tumour cells to undergo apoptosis cause resistance to chemoradiological therapies due to overexpression of oncogenes and transcriptionally repressed apoptotic tumour suppressor genes due to aberrant methylation (CIMP+).

Materials and Methods: We obtained surgically a total of 19 pancreatic cancer specimens from 12 males and 7 females (mean age 60 years) consisting of 9 ductal adenocarcinomas, 4 carcinomas of the papilla of Vateri, 1 acinus Ca, 1 neuroendocrine Ca, 1 intrapancreatic distal bile duct and 3 periampullary Ca. Genomic DNA of tumours was analysed for CpG island hypermethylation by using methylation specific PCR. All of the tumours showed hypermethylation of tumour suppressor genes with the following frequencies: DUSP6/MKP-3 88%, RASSF1A 80%, RARb2 70%, BRCA1 50%. Quantitative IHC, WB, SB and RT-PCR exhibited overexpression of DNMT1, CaSm, bcl-2, Raf-1 and cdc25c. We treated the samples with the isolated tumour cells with anti-CaSm scFv attached onto high energy- radioisotopes, vinorelbine-tartrate and 21-nucleotide double-stranded siRNA segment generated against DNMT1.

Results: Post-treatment, we detected re-expression of oncosuppressors DUSP6/MKP-3, RASSF1A, RARb2, BRCA1 after inhibition of DNMT1 mRNA. There was downregulation of antiapoptotic oncogene CaSm due to targeted scFv and inactivation of bcl-2, Raf-1 and cdc25c due to phosphorylation by vinorelbine. Furthermore, we detected upregulation of p21waf1, p27kip, Bid and Bak. The high energy radioisotopes induced DNA double strand breaks in tumor cells arresting synergistically with MT depolymerizing vinorelbine their growth at the G2/M transition according to flow cytometry analysis. We detected externalization of PS, depolarization of mitochondrial transmembrane potential ($\Delta\psi$ M), activation of caspase-3, caspase-7, 8, 9, bax, cleavage of poly(ADP-ribose) polymerase and DNA fragmentation. TEM exhibited irreversible D2 apoptotic signs forming apoptotic bodies indicating type I PCD after chromatin condensation and nuclear fragmentation. Overexpression of Beclin-1, PTEN, p70, DAPK and BNIP3 induced ceramide mediated autophagic cell death termed as type II PCD where LC3 is localized in autophagosome membranes. BrdU and MTT exhibited inhibition of DNA synthesis and metabolic activity of treated tumor cells compared to untreated controls.

Conclusion: We have achieved to eradicate pancreatic Ca cells with combined chemoradioimmuno-therapy after circumvention of chemo- and radioresistant mechanisms such as hypermethylation of oncosuppressors RASSF1A, RARb2, DUSP6/MKP-3, BRCA1 and overexpression of antiapoptotic oncogenes such as bcl-2, CaSm, Raf-1 and cdc25c.

34 THE EFFECT OF URSODEOXYCHOLIC ACID (UDCA) ON EXPERIMENTAL COLON CANCER IN RATS.

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Aim: To investigate the effect of various concentrations of UDCA on an experimental model of colon carcinogenesis in rats. The results of UDCA administration were compared with those observed in normal animals and animals receiving Cholic acid (CA) a well known carcinogenic agent.

Materials-Methods: Six groups of 6 male Wistar rats each were used. All animals were fed a basal diet, supplemented with 0.2% (group 2) or 0.8% (group 3) CA, 0.2% (group 4) or 0.8% (group 5) UDCA, 0.2% CA and 0.2% UDCA (group 6), and 0.8% CA and 0.8% UDCA (group 7) respectively. A group of 6 normal animals fed with basal (without CA or UDCA) were served as normal control group (Group 1). Two subcutaneous injections of azoxymethane were administered to groups 2-7 on the 1st and 15th day of the experiment, respectively. Animals were sacrificed at the end of 28th week. The rate of mucosal cellular proliferation was estimated by using the Proliferating Cell Nuclear Antigen (PCNA) assay. Tumour Necrosis Factor- α levels (TNF- α) in serum were also determined (U/ml: 1 Unit = 50pg cytokine).

Results: Histological alterations-Colon: Group 2: One animal developed a polyp and intramucosal carcinoma. The rest exhibited villous transformation of the mucosa. Group 5: In all animals a polypoid appearance of the mucosa was exhibited. One animal developed severe dysplasia. Group 6: Polypoid appearance of the colon was observed in 3 out of 7 animals. Group 7: All animals developed polypoid appearance of the mucosa and in one a metastatic lesion in a lymph node, was noticed. Differences in the various histological parameters between animals receiving UDCA and those receiving CA were statistically significant.

Small intestine: In all groups, thickening of the villi and increase in the cellular infiltration of lamina propria was observed. Although the most obvious alterations were observed on group 7, no significant differences between groups receiving azoxymethane and UDCA and those receiving CA and azoxymethane were found.

PCNA expression: The expression of PCNA was found to fluctuate with a relative increase at places of epithelial hyperplasia and places with polypoid appearance.

TNF- α levels: The levels of serum TNF- α were statistically significantly increased in all groups compared to the control group.

Conclusion: Ursodeoxycholic acid most possibly acts in a preventive way in this experimental model of colon cancer.

35 ALTERATIONS IN NUTRITIONAL STATUS OF GASTROINTESTINAL CANCER PATIENTS. A PROSPECTIVE STUDY OF 148 PATIENTS

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Aim. To record alterations in the nutritional parameters of patients with gastrointestinal cancer during their hospitalization in a surgical clinic.

Patients and Methods: This prospective study was performed in a teaching University Surgical Clinic. It enrolled patients that were admitted under the diagnosis of gastrointestinal cancer, and were submitted to surgical treatment. Collected data included different nutritional status parameters as: body weight, serum albumin concentration and blood total lymphocyte count. The data were recorded on admission and upon discharge of the patients from the hospital. Data concerning the clinical course of the patients, and their perioperative nutritional support were also recorded.

Results: In total, 148 patients included in the study (74 male – 72 female) during a one-year period. The median age was 67 years (range: 28-91). There were 83 patients with colon cancer, 34 patients with gastric cancer and 31 patients with cancer of the pancreas or the common bile duct. The mean weight loss per time unit on admission was 5.9% (SE: +/- 0.44). The mean values of the basic nutrition parameters, measured upon entrance and exit of the patients were: body weight: 68.0 to 65.7 kg ($p < 0.005$), serum albumine: 3.8 to 3.5 gr/dl ($p < 0.005$), lymphocyte count: 1790 to 1521/mm³ ($p = 0.028$). The duration of the hospital stay, the cancer site and the surgical complications were the factors with the greater influence at the alteration in the nutrition status of the patients.

Conclusions: Patients with gastrointestinal cancer are admitted for an operation with mild malnutrition. On discharge, their nutritional status is significantly deteriorated. It is possible that their compromised nutritional status delays their return to normal activity, and the onset of adjuvant therapy.

36 THE DIAGNOSTIC ACCURACY OF COMBINED INTRAOPERATIVE IMPRINTS AND FNA IN PANCREATIC SURGERY

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Background: We evaluated 27 series of intraoperative imprints and FNA specimens during pancreatic surgery.

Materials and Methods: Series of intraoperative imprints and FNA specimens of 27 patients who underwent pancreatic surgery during the last four years were taken. Eighteen of the patients were male and 9 female, aged 39-76 years. The main types of surgery were Whipple pancreaticoduodenectomy, pylorus preserving pancreaticoduodenectomy and distal pancreatectomy. All the intraoperative imprints and FNA specimen series were first diagnosed by HE rapid modified technique, followed by the Papanicolaou method. Imprints from the surgical margins were also taken. All cases were histologically confirmed. Imprints provide better cytomorphologic features by preserving well tumor architecture and sampling capacity, than frozen sections.

Results: From the 27 evaluated cases, 21 were diagnosed as adenocarcinoma, 5 as chronic pancreatitis, while the last one was suspicious of malignancy. When compared to the histology report the accuracy of both combined methods (FNA and imprints) was 96.9%.

Conclusions: The application of combined intraoperative FNA and imprint method has excellent diagnostic results. Its diagnostic accuracy is 96.9%. It is a rapid, non expensive and safe intraoperative diagnostic method in pancreatic surgery.

37 PROGNOSTIC EVALUATION OF CD44 EXPRESSION IN CORRELATION WITH BCL-2, P53 AND C-ERB-2 IN COLORECTAL CANCER

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Background: To investigate the expression of CD44 in colorectal carcinoma and examine its association with clinico-pathological features, bcl-2, p53, c-erb-2 and long term outcome.

Methods: Paraffin embedded specimens from 61 patients with Dukes's stage B (AJCC/UICC stage I) and 39 patients with Dukes's stage C (AJCC/UICC stage III) colorectal adenocarcinoma who were treated with surgery were assessed. We determined the expression of CD44, bcl-2, p53, and c-erb-2 with 5 year follow up.

Results: Low CD44 expression was present in 30%, moderate CD44 expression in 30% and extensive in 40% of cases. Expression of CD44 was unrelated to patient sex and age but was related to tumour differentiation, stage and tumour site. No association was demonstrated between CD44 and p53 in the 66 cases where p53 was previously assessed. There was a trend towards increased survival in patients whose tumours expressed lower percentages of CD44 protein. When entered into multivariate analysis model, which also included bcl-2, p53 and c-erb-2, CD44 staining emerged as a prognostic indicator variable.

Conclusions: CD44 expression may be an indicator of poor prognosis in colorectal cancer patients.

38 SPIRAL CT EVALUATION AND DIAGNOSIS OF SIGMOID COLON CANCER AND ITS LOCALISED EXTRA-COLONIC INVOLVEMENT

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Purpose: The purpose of this study is to establish the usefulness of spiral CT examination in the diagnosis and pre-surgical staging of sigmoid colon cancer.

Methods-Material: Sixty-seven patients were examined before and after peros contrast material administration. A PICK-ER PQ 5000 CT was used and 5-7mm thick axial slices were obtained.

Results: According to the CT findings the patients were divided into 3 categories:

I) Out of 32 patients with sigmoidal wall thickening and luminal narrowing, 31 also showed pericolonic fat involvement, while in 23 cases pericolonic lymph node enlargement was also observed. Extraluminal extension of the tumour was found in 19 of the 32 patients.

II) A sigmoid mass of soft tissue density with perisigmoidal fat involvement, stranding and extraluminal extension was observed in 29 patients. Twenty-seven of these patients were found to have mesenteric and pericolonic lymph node involvement. Nine patients also had distant enlarged para-aortic lymph nodes.

III) In 6 patients a small-degree stenosis of the sigmoid was observed. Two of them showed pericolonic fat involvement, while one patient had enlarged regional lymph nodes.

The CT findings were later proven correct after the surgical excision of the tumour.

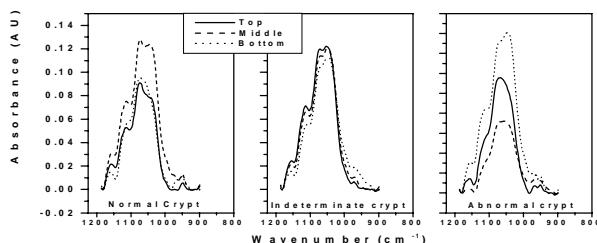
Conclusions: Spiral CT examination has a high resolution capability in the detection and diagnosis of sigmoid colon cancer and plays an important role in its investigation and staging.

39 ASSESSMENT OF ABNORMAL PROLIFERATION (PREMALIGNANCY) IN COLONIC RESECTION MARGINS USING FTIR-MICROSPECTROSCOPY

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Premalignant conditions in the colon have been associated with abnormal crypt proliferation. The detection of abnormal crypts is essential for diagnosis of spread of colon cancer and its effective management. It has been possible to identify abnormal crypt proliferation in colon tissues by various techniques. Among these, FTIR-microspectroscopy (FTIR-MSP) has been shown to provide important clues regarding the changes in the biochemical composition of cells and tissues especially during carcinogenesis. In the present work the growth pattern of the crypts has been undertaken to trace abnormal proliferation using FTIR-MSP. We studied the resection margins of colon cancer patients to identify abnormally proliferating crypts. The paraffin embedded tissues from the two sides of the resection were studied using FTIR-MSP and difference spectra were used to identify abnormal crypts. For each section, at least ten crypts from different regions were measured along the entire height. In addition, abnormal metabolism of other cellular components was also studied to confirm the abnormal, normal or intermediate nature of the crypt which display normal histology. The percentage of abnormal crypts identified with respect to the total number studied in each margin was used to assess the severity of the disease and cross checked with follow up histories to confirm the observation through clinical reports. The data shows that FTIR-MSP may be used to reassess the margins post operation, and give a complete prognosis for patients.



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40 ULTRASONIC DISSECTION FOR THE TRANSANAL RESECTION OF RECTAL POLYPS

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The treatment of choice for large sessile rectal polyps is a local resection usually carried out transanally. The procedure can be performed either with conventional transanal techniques or with the T.E.M. (Transanal Endoscopic Microsurgery) technology. Bleeding control during dissection usually is attempted with standard or high-frequency monopolar diathermy. In General Surgery, the introduction of the ultrasonically activated shears has improved the precision and quality of tissue dissection and this technology has been used efficaciously in transanal procedures as well.

During the last two years (2003-2004) we have treated seven patients with large rectal adenomas, using the ultrasonic scissors, in ten transanal resection sessions. The size of the lesions varied from 3 to 7 cm and the distance from the anal verge ranged from 3 to 13 cm. Two transanal resections were carried out using a T.E.M. gasless technique and the remaining eight were performed with conventional methods. In all these cases the dissection of the margins was carried out with ultrasonics scissors without the need of any additional hemostatic device. In three cases full thickness resection was carried out and the defect was closed with 3/0 polydioxanone sutures (in T.E.M. in a running fashion). No patient developed any postoperative bleeding or perirectal infection and they were discharged the second postoperative day.

41 THE TISSUE TAS (TOTAL ANTIOXIDATIVE STATUS) AS A CARCINOGENESIS MARKER IN THE POLYP OF THE LARGE BOWEL

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Purpose of the study: The aim of the research was to evaluate the Total Antioxidative Status (TAS) changes of the polyps tissue of the large bowel in relation to the pathological changes occurring in those polyps.

Material and method: The analysis included 73 patients, 43 men and 30 women aged 28 to 71 years, treated because of polyps of the large bowel. The materials for the study was made up of the tissue of 86 polyps removed endoscopically or surgically. In all the cases, beside the precise histopathological evaluation of the polyp structure, the estimation was also conducted of the TAS (Randox test) of the tissue material removed, referring the values obtained of the antioxidant state to the determined type of pathology of the large bowel mucosa. In evaluating the pathological changes the following points were differentiated: normal mucosa, inflammatory changes, dysplasia cancer. The statistical analysis was carried out using the STATISTICA 6.0 PL programme.

Results and conclusions. 1. In the large bowel the tissue polyps TAS decreases as the mucosa pathology increases.

2. Particularly deep deficiencies of the tissue antioxidants, however, occur only in the dysplasia and cancer of the large bowel (the average TAS drops by 5 times in the dysplasia) and by 18 times in the cancer in comparison with the normal mucosa of the large bowel).

3. The TAS study of the mucosa of the large bowel may be a valuable complement to the diagnostic panel used so far in evaluating the increase of the pathology of this part of the alimentary canal.

42 RISK OF GASTROINTESTINAL CANCER IN CHERNOBYL CLEAN-UP WORKERS

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The goal of trial is to compare the incidence of gastrointestinal cancer (GC) in Chernobyl clean-up workers (CCW) inhabitants of Latvia.

Method: This study used the data from Latvian Cancer and CCW Register of subjects affected during Chernobyl accident. CCW data were compared to controls (Latvian male population); the revealed difference was processed upon multifactor cluster Kulback analysis, Fisher's method.

Results: Totally 168 accidents (men; aged 35-70) of malignant tumours were being registered during 1989-2004. GC from all malignancies was revealed in CCW-31% and controls-21%. The next relative morbidity rate of some kinds of GC was revealed: stomach (SC)-44%, colorectal (CC)-23%, oral cavity-13,5%, esophageal-11,5%, pancreatic-4%, and hepatic cancer-4%. But regular population's morbidity relative rate appears to differ from mentioned above. SC rate in CCW increased in 2,5 times but CC rate - in 4 times during 2000 - 2003 being compared to healthy controls. No convincing difference was found analysing other forms of SC in CCW, when compared to the control.

Those CCW who has been taken part in clean-up works in 1986 received greater radiation dosage and morbidity rate in them is higher than in group who served in 1987-1988 and received a lower dosage of radiation. Oncological morbidity rate obviously rises when 5-9 years after radiation was received. In case oncology has been revealed during this term of 5-years past-term, lethal exit's probability statistically is much higher. In case of 15-years past-term much more patients survive. A risk of oncology is statistically aggressively higher in a group of CCW of age 30 and younger (at the moment of clean-up working) comparing to a group of older workers. CC morbidity rate is statistically higher in case of radiation dosage was less for 1 Gr but in patients of age 45 and older.

Conclusions:

1. The dosage of radiation received by CCW influences on GC epidemiology.

2. SC and CC incidence rate appear to be the highest one.