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PROGNOSTIC SIGNIFICANCE OF FLOW CYTOMETRY (FCM) AND IMMUNOCHEMISTRY (IC) IN COLORECTAL CANCER (CCR).

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We review a retrospective study about the prognostic significanceof ploidy, proliferative activity (S-Phase) and P-glicoprotein (P-gp) expression in comparision of clinical prognostic markers(PM) like age, sex and site or pathological PM like grade, stage histological type and vascular and perineural invasion inpatients (pts) with CRC. Ploidy was analysed in 105 pts. There was 57% of aneuploid tumours and 41% of diploid. The S-phase could be calculated in 91 pts with 42% with S phase values under the median (11,3%) and 43% over it. P-gp expression was positive in 57% of primary tumours, in 59,4% of lymph nodes and in 53,9% of metastases. In univariate analysis (mantel cox test) the survival (S) was significantly related with sex, stage, vascular invasion,ploidy and S phase. The result was the same for the relapse-free survival (RFS) save the sex.
In multivariate analysis (cox-regresion model) the S abd the RFS were significantly related with stage, vascular invasion and ploidy with a higher risk of death and recurrence in pts with stage C and D (Dukes staging), with vascular invasion and aneuploid tumours.
The stage, the vascular invasion and the ploidy are independent PM for the S and the RFS of pts with CRC. They should play an importantin the selection of pts for the adjuvant treatment. P-gp expression and S-phase are not PM in CRC. Sex, age, histological type, site grade and perineural invasion are not PM in CRC.

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HYPERFRACTIONATED RADIOTHERAPY AND TEGAFUR IN LOCAL RELAPSE OF ADENOCARCINOMA OF THE RECTUM:A PILOT STUDY

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There is experimental and clinical data that Tegafur, a fluoropyrimidine analogue, may act as a radiosensitizer. Between 3/88 to 10/89 we conducted a pilot study to evaluate toxicity and efficacy of hyperfraccionated radiotherapy (115 cGy,twice a daily,5 d/w) and concomitant peroral administration of Tegafur (1200 mg/day) in a poor prognostic group of patients(pts) with a nonresectable local relapse of adenocarcinoma of the rectum.Patients characteristic: 10 pts were entered into study.Mean age 55.6 (range:33-66);3 males,7 females;Karnofsky range 60-90%;mean radiation dose 52.5 Gy (range:31.4-67.8).Toxicity was evaluated by WHO criteria.Results:Toxicity in general was mild and well tolerated. Hematologic complications grade (gr) 1-2 were present in 4 pts. Only 1 pt developed major hematologic toxicity (leukopenia gr 3). Other toxicities: nausea/vomiting gr 1-2 (2 pts),diarrhea gr 3-4 (2 pts), epithelitis gr 1-2 (5 pts).The response rate for 7 pts evaluable was 42% (0 CR,3 PR). 4 pts had stable or progressive disease. The median duration of response was 9 months. Conclusions: In this pilot study hyperfractionated radiotherapy plus Tegafur were well tolerated, but not improvement of the expected response rates from conventional radiotherapy treatment was observed.

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INTESTINAL RADIATION DAMAGE AFTER RADIOTHERAPY AND CHEMOTHERAPY (EXPERIMENT ON DOGS)

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Ten beagle female and male dogs, weight 10-12 kg, 1-2 yrs old, were irradiated with 25 Gy (Cobalt-Phillips) onto the whole pelvis and tail for 20 days. Platinol was given in a 2-hr infusion every 5 days for 20 days during radiation treatment. Ten dogs represented a control group. The 3rd group of dogs was also treated by irradiation and chemotherapy, but with a special diet containing low protein and some cations and anions. Ten days after completed experiment, the thoracic duct lymphocytes, peripheral blood and the large intestine were examined with the following parameters: laboratory-, biochemical-, histochemical, EM-, SEM-, densitometric-, immunological-, LAMMA 500 and immunohistochemical ABC (avidin-biotin complex) method for serotonin and somatostatin determination. Damage and remodelling of peripheral blood lymphocytes, thoracic duct lymphocytes, entero-endocrie-, mast cells and lymphocytes in the intestinal smears of the lamina propria were found in all treated dogs. There were significant differences between the treated and control group of dogs. Forty patients with radiation-related intestinal damage and surgical treatment will be presented.

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5-FLUOROURACIL (5FU) PLUS LEVOFOLINIC ACID (l-FA) AND HYDROXYUREA (HU) ON A WEEKLY SCHEDULE IN THE TREATMENT OF METASTATIC AND/OR RECURRENT COLORECTAL ADENOCARCINOMA (CA).

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After informed consent 22 pts with advanced CA have been enrolled to date. There were 12 females and 10 males with a mean age of 63 years and a mean KI of 75. Twenty pts had previously received surgery, 3 RT and 10 had CT with 5FU alone or 5FU plus rIFNa2 or FA. 18 pts had primary tumor in the colon and 4 pts in the rectum. Sites of disease included : liver (10 pts), lung (3 pts), abdomen (10 pts), node (1 pt). Treatment plan was : l-FA 100 mg/m2 i.v. in 250 cc of NS plus 5FU 450 - 600 mg/m2 over 1 hr infusion; HU 1000 mg/m2 p.o. in 3 doses starting 6 hrs after lFA-5FU infusion was ended. This treatment was given weekly for 6 consecutive wks followed by a 15 day rest period. One pt with nodal metastases had a CR after 1 cycle, while a PR has been recorded in 5 cases for an ORR of 27%. This regimen has been very well tolerated with grade 2 leukopenia in 3 cases (13.6%), and grade 3 diarrhea in 4 pts (18%). Mild stomatitis (G1) has been observed in 4 pts (18%). These results, although preliminary, suggest that HU may further modulate 5FU cytotoxic activity without increasing gastrointestinal toxicity. The study is still open.

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THE RATIONALE FOR CEA DOSAGE IN THE FOLLOW-UP PATIENTS OPERATED FOR COLORECTAL CANCER.A PROSPECTIVE STUDY OF 800 CASES.

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The purpose of follow-up studies in resected colorectal cancer is early detection of recurrent disease at a stage still accessible to surgical treatment. Between 1975 and 1988 a prospective study was carried out on 800 patients with a curative resection. Only 322 patients (40.2%) consented to undergo a scheduled follow-up study (Group I) whereas the remaining 478 patients (Group II) were reviewed on an occasional basis or because of symptoms. Results were as follows : 1) recurrent disease was found in 92 cases of Group I representing 34.5% of 267 recurrences occured in the whole series of 800 patients. 2) CEA was the most accurate test in the detection of recurrent disease allowing diagnosis in 77% of cases(97% for liver metastases).3) surgical resection of recurrent disease was performed in 32.6% of patients in Group I versus 8% in Group II(p<0.001).4) the 5-year survival rate of resected recurrent disease was 10% in Group I versus 8% in Group II (p<0.01). The analysis of these results underlines the radionale for serum CEA in early detection and surgical treatment of recurrent disease.

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LAPAROSCOPIC GUIDED BRACHYTHERAPY IMPLANT INSERTION FOR RECTAL CANCER.

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Polyethylene tubes for brachytherapy implants were inserted in three patients with rectal cancer. one patient had metastatic disease and two patients refused surgery for the resection of the tumor. Laparoscopy was performed under general anethesia. The bowel and pelvic content were retracted via a separate trocar and the polyethylene tubes were placed through the perineumguided by laparoscopy to avoid injury to intra-abdominal organs. The patients did not require a nasogastric tube postoperatively, and the polyethylene tubes were loaded with radioactive implantson the first or second postoperative day. all patients received 5000 Rad with satisfactory results and no complications. They all left the hospital following completion of therapy.
We conclude that laparoscopy is a vluable tool in aiding theplacement of brachytherapy implants for rectal tumors, and possibly for other pelvic and intra-abdominal locations.