necessary for oncological reasons. Reconstruction of the sphincter function is achieved using a seromuscular cuff. This procedure avoid an abdominal colostomy. The neosphincter can also be formed secondarily, after a prior abdominoperineal excision with transabdominal colostomy. Quality of life will be improved, especially if an artificial anus can be avoid.

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Radiotherapy of early localised rectal cancer

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Purpose: To evaluate the role of radiotherapy alone for cure in the treatment of "early" rectal cancers with 2 different approaches.

Patients and treatment: Between 1980–96, 149 patients divided in 2 groups. *Group A:* 106 pts with T1 and early T2N0 treated with endocavitary irradiation alone. Median dose of contact x -ray 95 Gy (4–5 fractions) and iridium 192 implant as a boost in 29 pts (25 Gy/1 day). *Group B:* 43 pts with T2-3 NO-1 in inoperable patients treated with contact x-ray (70 Gy/3 F) followed by external beam radiation therapy: 39 Gy/13 F/17 days + 4 Gy concomitant boost and iridium 192 implant (20 Gy/1 day).

Results: *Group A:* overall and specific 5-year survival was 83% and 94%. LOCO-regional failure were seen in 15 pts (12 were salvaged). *Group B:* overall and specific 5-year survival was 68% and 74%. Loco-regional failure were seen in 32 pts (72%). no grade 3 complication was observed.

Discussion: Surgery remains the basic treatment of rectal cancer. In highly selected cases irradiation alone can cure early T1-2 NO tumors and in inoperable patients some larger T2-3 tumors.

[1] Ref. J.P. GERARD Int. J. Rad. Oncol. BP (1996) 34: 775–83
[2] Rad. Oncol. 1996-38: 131–37

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The surgeon and surgical procedure as a prognostic factor

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The outcome of surgery for colorectal cancer varies between surgeons. Although there may well be selection bias in the cohort studies which indicate this effect, some single institution data exist to support this contention. The range of difference between surgeons in post operative complications, local recurrence and survival is larger than any likely effect of presently available adjuvant therapy.

Assuming no selection bias, surgeon variation must be due to differences in surgical technique sufficient to translate into different outcomes. Despite the likely size of this effect there have been almost no prospective randomised studies in this field. At present the two areas of technique which may be important variables are extended pelvic lymphadenectomy, as promulgated mainly by Japanese surgeons, and Heald's technique of total mesorectal excision. It is likely that both these approaches contain all the elements of best surgical practice; it is also likely that they are more radical than is necessary to produce optimum oncological outcome, with functional side effects that might be avoidable by lesser procedures It should be a matter of high priority for surgeons to design and perform prospective comparative trials to answer some of these important questions.

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Camptothecins

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Camptothecins (C) are a new class of antitumor compounds which act through inhibition of topoisomerase I, an enzyme crucial for changes in the topology of DNA during replication. The initial step for the induction of cell death by these agents is the formation of a stable DNA-drug-topoisomerase I complex (DDTC) during S-Phase. A fork-collision model has been developed to explain cell cycle phase specificity and implies the irreversible arrest of moving replication forks by the DDTC. Although the parent compound camptothecin showed promising activity in preclinical models, subsequent clinical trials yielded unacceptable toxicities Subsequently, analogues [irinotecan (CPT-11), topotecan, GI 147211, 9-amino-camptothecin, 9-nitro-camptothecin] have been developed and are now in various stages of clinical evaluation. Oral formulations of C are also under investigation. CTP-11 is clinically active against colorectal cancer and is currently evaluated in combination regimens. Topotecan and GI 147211 are active in ovarian and small-cell lung cancer. 9-amino-camptothecin and 9-nitro-camptothecin are currently being evaluated in Phase I trials. Other analogues are in preclinical evaluation. C are promising new agents with a unique mechanism of action, peculiar clinical pharmacology, and widespread clinical activity which will become part of the standard armamentarium of the practicing oncologist in the future.

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Marine organisms – Are they a worthwhile source?

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Forty years ago, Pettit and colleagues began a search for novel antineoplastic agents in marine organisms, which represent a life form of extraordinary longevity (over 3 billion years). Cancer is unknown in these animals, and the hypothesis is that their survival results from the evolutionary development of complex chemical protective agents with potent antiproliferative activity. More recently this search has been extended by specialist companies such as Pharma Mar SA. A large number of peptides have been isolated from a range of organisms, including the tunicates, sponges, bryozoans and algae, and shown to possess a high degree of antitumour activity in preclinical screens, including those involving human tumour xenografts. Several compounds have already reached clinical trial. These include the protein kinase C modulating agent bryostatin I, which was found in Phase I trials to have activity in melanoma, non-Hodgkins lymphoma, ovarian and cervical cancer, the protein synthesis inhibitor, didemnin B, with activity in glioma, and the antimicrotubule agents LU 103793 (a synthetic analogue of dolastatin) and ecteinascidin-743. Toxicities seen include myalgia (bryostatin), vomiting (didemnin B) and myelosuppression (LU 103793). Bryostatin-I is the most advanced in clinical assessment, and Phase II trials are proceeding. The preliminary signs of clinical efficacy, together with the wealth of novel structures in the development pipeline, gives rise to optimism that the sea will indeed prove to be a worthwhile source of anticancer agents.

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Matrix metalloproteinase inhibitors

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Matrix metallo proteinases (MMPs) function in the degradation of extracellular matrix proteins that constitute connective tissue. In cancer there appears to be a local and temporal imbalance between the levels of activated enzymes and their inhibitors. This imbalance results in a break-down of the extracellular matrix. Degradation of the extracellular matrix is necessary when invasive tumor cells penetrate tissues, gain access to blood vessels, exit blood vessels and colonize distant sites. Thus, inhibition of the process might result in prevention of cancer progression. For this purpose synthetic matrix metallo-proteinase inhibitors (MMPIs) have been developed. In preclinical studies they were shown to inhibit organ colonization by tumor cells as well as lymphatic spread. The resultant was increased survival. In addition, there are data that MPIs are additive to the effect of cytotoxic drugs. Clinical studies up to now have been limited. Local intraperitoneal or intrapleural administration of batimastat resulted in postponement of necessary drainage procedures, but especially the intraperitoneal application was limited by to local side effects. For this reason, the present focus is on MPIs with appropriate oral bioavailability. Marimastat is the first example of an orally available MPI that was extensively studied, CGS 27023A recently also entered clinical studies. Efficacy data on MMPIs will be reviewed.

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Compounds inhibiting angiogenesis

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The dependency of tumour growth on a vascular supply is established. Shutting off the supply route would lead to tumour necrosis, preventing its development would lead to growth inhibition, both at primary and secondary sites. Accessibility of vessels for systemically administered compounds, the small (or absent?) chance of resistance development and the projected limited toxicity of agents directed at a quiescent cell population, are highly promising. These two types of anti-vascular treatment need to be distinguished. The first aims at selective tumour vessel destruction and