

WEDNESDAY 17 SEPTEMBER 1997

Teaching Lectures

635

Conservative treatment of breast cancer: When, how, and who?

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Breast-conserving treatment of small breast cancer has gained wide acceptance in the recent years, following the results of large trials. The standard treatment combines a wide surgical excision followed by breast irradiation. Typically, it applies to small unifocal tumors, either in situ or invasive, and must comply to two principles: to obtain clear margins, and to preserve breast cosmesis. The role of radiotherapy has been challenged recently. We will review the results of trials that have tried to determine whether radiotherapy could be omitted in some instances.

The increasing and earlier use of adjuvant systemic treatment in breast cancer has changed the strategies of breast-conservation, which is now offered to patients with large tumors. Upfront chemotherapy or radiotherapy can be used to downstage the primary tumor, allowing breast-conserving surgery in a second step. However, many questions remain regarding the most efficient treatment sequences. Finally, not all patients can benefit from breast-conserving treatment. Criteria for breast-conservation need to be defined, based on psychological, clinical and biological parameters, and on the identification of prognostic factors on long term results.

636

Colorectal surgery – How do I do it?

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Between 2/92 and 12/96 1016 (183 resections tumor recurrence included) colorectal operations were performed.

Out of them 887 patients were operated because of colorectal cancer. Operative techniques are standardized, so that our results meet the data, which are published by several groups concerning survival, complications (4.6%), R0-resectability (73.3%) and lethality (2.5%).

In 37 patients the resection of the colorectal carcinoma was simultaneously combined with a liver resection because of synchronous hepatic metastases. This group did not differ concerning long term survival compared to patients after hepatic resection because of metachronous liver metastases of colorectal primaries.

In comparison to patients, which had only a colorectal resection the group of patients with simultaneous colorectal and hepatic resection had no increase of postoperative complications. Therefore we recommend a simultaneous hepatic and colorectal resection for patients with colorectal cancer and resectable synchronous liver metastases.

637

Signal transducers as molecular targets for cancer therapy

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The c-MET oncogene is the prototype of a family of tyrosine kinase receptors known to control invasive cell growth. Activation of c-MET induces cell-cell dissociation, motility and invasion of extracellular matrix. These effects are mediated by phosphorylation of the tandemly repeated sequence (YVN/HV) located in the C-terminal tail of the receptor. This sequence binds a number of SH2 containing signal transducers including Grb2, p85 and src and concomitantly activates multiple signaling pathways. By molecular modeling of this region we have identified peptides interfering with binding of SH2 proteins to the Met receptor. Four aminoacid peptides were required to interfere with binding of p85 and src, surprisingly however, the small peptide YVN (1/2) was sufficient to bind the SH2 domain of Grb2. Peptide derivatives, resistant to proteases and tyrosine phosphatases, were ob-

tained by modification of the phosphate moiety and of the C and N terminal aminoacids. One of these molecules, Ac-mPYVNV-NH₂ interacts with high affinity with the SH2 domains of Grb2, p85 and src. This derivative can also prevent binding of the full-size Met receptor to the above transducers. Upon introduction into cellular systems Ac-mPYVNV-NH₂ specifically inhibits Met mediated biological effects including cell dissociation, motility and invasion of extracellular matrix *in vitro*. This data demonstrate that peptide-mimetics interfering with Met signal transduction can be efficiently used to prevent invasive cell growth *in vitro*.

638

Update on recent developments in cancer pain management

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The author wishes to summarise the most recent developments in cancer pain management. In research regarding routes of administration of opioids alternatively to the oral route, the rectal administration of morphine and methadone and the transdermal route for fentanyl have proved to be efficacious. Various studies suggest that alternative routes are necessary in 53–70% of patients in the last days or months of life. The most frequent causes for the need to suspend oral administration are dysphagia, nausea, and uncontrollable vomiting, bowel obstruction, malabsorption, cognitive failure, coma, and pain syndromes requiring anesthetics which need be administered via the spinal route. Among the drugs used the author will present an experience on the use of methadone in 196 patients. Tramadol is a new drug for Italy and seems to be effective in the control of moderate pain. It is a centrally acting analgesic drug; it has an agonist effect on mu 1 receptors of opioids and acts also by inhibiting the reuptake of noradrenaline and serotonin which activates descending monoaminergic inhibitory pathways. Recent clinical studies revealed that pamidronate has an analgesic effect in pain due to bone metastasis. Pamidronate is part of the bisphosphonates, which are active on bone metabolism and are usually being used for the treatment of hypercalcaemia in cancer. The author also describes briefly the indication of Ketimine, a drug with anaesthetic and analgesic properties, in association with morphine for the treatment of neuropathic pain.

639

Multi modal cancer care – The role of the surgeon

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In order to retain a central role in the management of patients with cancer, the training and practice of the surgeon must be developed. Surgeons who treat cancer should nowadays be required to have (1) technical competence in cancer operations (2) involvement in peri-operative and outcome audit (3) ability to assess the value of new technology (4) understanding of clinical trials and involvement in guidelines of care (5) an ability to evaluate other modalities of cancer treatment (6) responsibility for follow up of cancer patients (7) ability to analyze the literature in oncology (8) an understanding of tumour biology (9) concern with clinical or laboratory research (10) organizational skill (11) the ability to work as a member of a multi-disciplinary team (12) continuing empathy in guiding patients through complex illnesses and (13) an undertaking to be the guardian of the patients' interests.

Such requirements can be developed by (a) recognition of surgical oncology as a specialty or sub-specialty within surgery (b) the establishment of a system of training in surgical oncology (c) the establishment of a qualifying examination in surgical oncology by way of the European Board of Surgery Qualification (EBSQ-onco) and (d) insistence on inter-disciplinary training for all medical personnel who treat patients with cancer.

The European Society of Surgical Oncology is promoting the establishment of a network of "Centres of Excellence" within Europe to facilitate exchange of trainers and trainees among cancer centres in Europe, ultimately leading to a system of accreditation of surgical oncologist in Europe.