

WEDNESDAY 15 SEPTEMBER 1999

Teaching Lectures

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Hodgkin's disease (HD). Prevention of long-term side effects

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Twenty years after therapy for HD, the mortality linked to long-term side effects or complications is grossly superimposable to the one which is directly related to the disease. So, prevention of long-term side effects is nowadays one of the main challenge for those patients.

Two different types of late effects should be considered: stochastic and deterministic.

The stochastic effects mainly correspond to secondary cancers. Secondary leukemias have been shown to be essentially related to the use of nitrogen mustard (chloromethine): in 1999, this drug has been almost unanimously abandoned.

Secondary solid tumors have been essentially related to radiotherapy. The progressive abandonment of the systematic large-field irradiations and the dose decrease (both made possible by the association with chemotherapy) should have already reduced this risk. In addition, several ongoing trials are being investigating the use of chemotherapy alone in advanced stages (III–IV), and even for some selected limited stages (I–II).

Late deterministic effects mainly correspond to long-term non-malignant complications of radiotherapy. Apart from the abandonment of irradiation for some selected cases (see above), a number parameters can (and should) be adapted to avoid – or at least to significantly reduce – those late deterministic effects: use of proper machines, reduction of the irradiated volumes, dose decrease, adequate fractionation and comprehensive quality assurance programs.

Actually, most of these changes have been progressively introduced since a decade. Recent historical comparisons seem to show that they have already significantly reduced the risk of long-term side effects and complications of Hodgkin's disease therapy.

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Is there a role for tumour markers in the management and follow-up of cancer patients?

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To answer this question appropriately, a disease-specific approach is necessary and a differentiation between management (therapy control) and follow-up. In germ cell tumors, tumor markers are of exceptional value for both management and follow-up. Lung cancer is an example for the uselessness of tumor markers in both settings. The reason for this is that therapeutic consequences are nil once a patient with lung cancer does not respond or relapses, while there is even curative therapy available for patients with germ cell cancer. In many other diseases such as breast cancer, cancer of the GI tract, prostatic cancer tumor markers may have a diagnostic role but – due to therapeutic limitations – only a poor role regarding therapy control and follow-up. In some instances (cancer of the ovary) tumor markers are more sensitive to evaluate therapeutic effects than imaging methods. When relating tumor markers to response steepness of decline, tumor heterogeneity, tumor lysis and catabolism and excretion of tumor markers have to be taken into consideration.

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Modern radiotherapy (RT) for medical oncologists and surgeons

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The "sectional imaging revolution" (70ies/80ies), which has been followed by the "3D treatment planning revolution" (90ies) is now being translated into clinical practice by the introduction of "3D conformal radiotherapy" (3DCRT), which applies both for external beam and brachy-therapy. A

specific application has been cranial stereotactic RT (SRT), which is now followed by extracranial SRT. All these approaches mean improving the therapeutic ratio by maximum sparing of normal tissue (decrease of side effects) and maximum adaptation of radiation to the target (increase of radiation dose and effect). Advanced computer technology (incl. networking) and advances in accelerator technology (MLC and IMRT) represent the major components in this rapidly evolving field. Advanced computer assisted modelling in clinical radiobiology provides efficient tools for the upfront assessment of tumor control and normal tissue complication probabilities (TCP, NTCP), which will soon lead to a "4D treatment planning revolution". In order to further improve the efficacy of radiotherapy, a tumor biology based approach "unconventional fractionation" (e.g. hyperfractionated accelerated RT) has been successfully introduced into some clinical settings. Recent radiobiological findings in different areas as "radiation induced apoptosis", "hypoxia", "cloning of human DNA repair genes", "identification of radiation mediated signal transduction pathways", will lead to novel treatment approaches, as e.g. radio-gentherapy. Combination radio- and chemotherapy (hormonal treatment) in a simultaneous or (neo)adjuvant setting with or without (organ conserving) surgery is one of the most promising approaches at present, for a variety of tumor sites like breast, prostate, lung, rectum, anus, lymphoma, head and neck, cervix uteri, pancreas. The next step to go will have to integrate these combination treatment concepts and the widely available modern radiotherapy tools (3DCRT, SRT), in order to further increase the therapeutic ratio. Improvements in supportive care (e.g. cytokines, radioprotectors) will facilitate this process of integration.

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Palliative treatment in advanced colo-rectal cancer

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The majority of patients with advanced colorectal cancer have an incurable disease. However, since the best chance for permanent cure is a second surgical attempt to remove all visible disease, all patients have to be evaluated for such a procedure. Surgery for local recurrences, liver metastases and lung metastases is worthwhile and must be considered in every case.

If the investigation has discovered an incurable disease, i.e. multiple lesions not suitable for resection, the next step is to evaluate whether or not any symptoms have to be palliated. Since there is no good "second" line therapy it is important to make a contract with the patients. Palliative treatment with chemotherapy or radiotherapy is often worthwhile but has to be used with cautious. Available data do support an early start of chemotherapy, both in terms of prolonged survival and quality of life. However, it is important to consider that symptoms must be palliated. With turnout markers it is possible to predict the response of chemotherapy. As soon as there is an indication of a weak response of chemotherapy, the patients must be informed and the treatment must be stopped. It is also essential not to use too "strong" drugs since in the palliation situation quality of life is the most important endpoint.

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The multidisciplinary approach for treatment of sarcomas

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Significant progress has been made in the management of patients with sarcomas. There has been increasing knowledge on the molecular biology and cytogenetics of sarcomas, and an importance of genetic factors in their development has been suggested. New histopathology techniques have been developed especially within the area of immunohistochemistry. There has been a marked change in quality of diagnostic imaging by introduction of CT and MR. In some of the sarcomas there has been a dramatic gain in survival due to the efficacy of multi-drug and multi-cycle chemotherapy protocols. However, one of the most important factors in their