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 (chlormethine): 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 controll and follow-up. In some instances (cancer of the ovary) tumor markers are more sensitive to evaluate therapeutic effetcs 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 acelerated 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 presetn, 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 knowlegde 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

treatment is the necessity of treatment planning within the framework of a multidisciplinary approach, which has been acknowledged by an increasing number of sarcoma centres. In soft tissue sarcomas (STS) local treatment is still of utmost importance for cure. However, the treatment has shifted from radical to more extremity saving procedures by the use of combined surgery and adjuvant radiotherapy, thereby improving the functional outcome and probably also quality of life. In locally advanced STS other modalities such as hyperthermia and local perfusion are being studied. The role of adjuvant chemotherapy is continuously debated. A recent meta-analysis showed an improved disease free survival but no effect on overall survival. Therefore, the results of ongoing randomized studies should awaited. In patients with metastatic disease only few cytostatic drugs are active, and new drugs are under investigation. In contrast, in Ewing,s sarcoma (ES) and osteosarcoma (OS) chemotherapy is a must in the primary treatment. In ES local treatment includes surgery and radiotherapy especially in non-bulky and chemoresponsive tumours. In OS the surgical procedures increasingly allow extremity saving procedures whereas radiotherapy is generally only used for palliation. Trials studying the optimal chemotherapy of ES and OS are ongoing, and hopefully a pan-European trial on ES will be initiated in the near future. The treatment strategy of advanced ES/OS has not been settled. Thus, although definite progress has been made within the field of sarcomas, continued efforts in studying these diseases are unequivocally needed.

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Cancer registry and cancer control

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Cancer Control consists activities that reduce occurrence of, suffering from or death from cancer. Such efforts assume good information background, which is usually called cancer registry. Cancer registry helps in cancer control practice, first, by providing information on the magnitude of the cancer problem at the population level. Such data are used for planning of the cancer services in the future and for setting of priorities within oncology and between the health sectors. Second, cancer registry evaluates the success of control measures at population level on primary prevention by incidence trends, on clinical activities by nation wide survival trends and on screening activities. Cancer registry is also a research institution which carries epidemiological research, health services research and collaborates in clinical research e.g. in terms of randomization center and analysis of RCT's.

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Abstract not received.