

Whipple group it was 12.1 months. The 5-year survival rate after tumor resection was 9%.

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Radiation oncology in pancreatic cancer

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Radiation therapy has been utilized in the care of patients with pancreatic cancer in two clinical settings: 1. as "definitive therapy" for unresectable or locally advanced non-metastatic disease and 2. as adjuvant or neoadjuvant therapy in resectable tumors. This presentation will review past and current data assessing the role of radiation therapy in conjunction with 5-fluorouracil based chemotherapy in these two clinical settings. Recent efforts combining irradiation with taxanes and gemcitabine will also be discussed.

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Developments in systemic therapy of pancreatic cancer

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Adenocarcinoma of the pancreas is a profound therapeutic challenge. Only a small fraction (about 3%) of patients with this disease will survive more than two years. In general, pancreatic cancer (PC) is considered to be a chemoresistant disease. It has been difficult to identify chemotherapy agents that have substantial efficacy as evidenced by objective tumor regressions or prolonged survival. For technical reasons localized PC is difficult to measure using 3-dimensional imaging; thus, novel surrogate endpoints must be explored such as reduction in circulating tumor associated antigens such as CA 19-9 or in improved quality of life or symptoms. The latter approach was used to define efficacy and gain FDA approval for gemcitabine (2'-deoxy-2'-difluorocytidine) in the U.S. This interesting compound is a prodrug which undergoes intracellular metabolism to active phosphorylated moieties. The accumulation of these metabolites is dose and dose-rate dependent; clinical studies evaluating this are in progress. Other new approaches for systemic therapy of PC are based on the molecular, biochemical and structural findings in PC. Identification of tumor antigen phenotype has spawned trials of radioimmunoconjugates and tumor vaccines. A molecular hallmark of PC, a mutated Ras oncogene, has encouraged the development of new drugs that inhibit farnesyl transferase activity, an important enzyme in Ras activation. Another approach involves matrix metalloproteinase enzymes which can degrade tissue extra-cellular matrix interfering with tumor invasion, neovascularization, and metastases.

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Imaging processing for evaluation and reduction of geometrical uncertainties in prostate irradiation

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The three major sources of geometrical uncertainties in radiotherapy of prostate cancer are: target volume delineation, organ motion, and patient set-up. Using image processing techniques, these uncertainties have been quantified in three dimensions and reduced. Usually the whole prostate is the target, making target volume delineation relatively easy compared to other tumour sites. All errors introduced at this stage are purely systematic, i.e., they influence all treatment fractions. In a pilot study, automatic image registration was used to include MR in the treatment planning process. It was found in an inter-observer study with three observers using CT and MR of 18 patients that the systematic differences between the target volumes delineated in CT and MR are significantly larger than the inter-observer variation. For example, the average target drawn on MRI has a 30% smaller volume compared to CT (a systematic difference of about 8 mm at the posterior aspect). Prostate motion has been studied using image registration of repeat CT scans. An advantage of this approach is that the motion of the prostate can be directly related to the volume of other organs such as the rectum or the bladder. In this study of 11 patients in 4 scans, the largest motion was a rotation around a left-right axis near the apex with a standard deviation of about 4 degrees. The prostate motion was found to be strongly correlated to rectal volume differences. In our clinical protocol, patients instructions to have empty therefore now re-scanned if the rectal volume

exceeds 150 cm³. In this way, large systematic errors in the prostate position (introduced by the planning CT) are eliminated. Finally, patient set-up has been studied using electronic portal imaging. In our institute, the set-up deviations are 2 mm standard deviation (for each axis) both for day-to-day variations and for systematic deviations. Without any correction, the vector length of the systematic set-up error exceeds 5 mm for 30% of the patient population. Using off-line image analysis and a simple decision protocol, virtually all systematic set-up errors exceeding 5 mm have been eliminated with relatively low workload: about one third of the fractions is imaged, while on average less than one correction per patient is performed. Using newly developed image processing tools, the set-up error has been quantified in 3-D, i.e., including all rotations. It was shown that the magnitude of the rotations is less than 1 degree standard deviation for all three directions. The combined effect in 3-D of the three geometrical uncertainties will be shown on clinical data on a video.

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Advances in conformal therapy

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During the last two decades major changes have taken place in radiation oncology: the "imaging revolution" of the 70ies/80ies is being followed in the 90ies by the "3 D treatment planning revolution" which means 3 D assessment of anatomy and optimization of dose distribution for target and critical organs using specific tools for estimating tumor control and normal tissue complication probabilities.

Conformation Radiotherapy (CR), which converts 3 D treatment planning into clinical radiotherapy, is the adaptation of the volume treated by radiation to the target volume, as precisely as possible, with maximum sparing of normal tissue. Although this aim has been pursued for decades, a high degree of conformation has become only possible within wide clinical use by recent developments in medical linear accelerators (multileaf collimators) and computer technology including networking. CR in clinical practice means at present multiple static fields (4-6), each shaped according to the individual target. Acute and long term adverse side effects are dramatically reduced by this technique. On the other hand, radiation dose escalation has become possible, resulting in a higher degree of (local) tumor control with acceptable radiation related morbidity. The most common tumor sites treated at present by CR are prostate, gynecology, liver, lung, base of the skull, brain, with very promising clinical data reported so far.

CR represents one of the most important tools for improving the therapeutic ratio in present and future radiotherapy.

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The European quality assurance program in radiotherapy

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The concept of Quality Assurance (QA) has recently broadened from its restricted definition of technical maintenance of equipments and treatment delivery toward a comprehensive approach of all activities in the radiotherapy department, from the moment the patient enters it until the moment he leaves, and even later during the follow-up. The comprehensive approach is favoured because it is recognised that partial organisation of some key steps in the radiotherapy process is not sufficient to guarantee the patient (and society) that each individual will receive appropriate optimal care for his/her disease. Also, besides the important technological aspects of radiotherapy, more emphasis has been recently put on QA of treatment indications, of treatment protocols, of treatment reporting and of systematic registration of side-effects and complications.

A comprehensive QA system reduces the likelihood of errors and accidents, it ensures continuing quality improvement, it increases efficiency, it raises staff morale and introduces a cultural change, it reduces the chance for litigation and it is a management tool.

The structure of such a system has been extensively discussed in the report "QA in radiotherapy" (R&O, 35: 61-73, 1995). The practical implementation of the principles, however, needs a specific methodology, which constitutes the project on which the ESTRO commission for QA has been working for the past 2 years. The report on this methodology will be discussed.