

than 100 in volume. Neglect of heterogeneity in tumor volume reduces the power of a study considerably. Thus, clinically relevant effects can be overlooked if tumor size is not taken into account. As compared to presently applied predictive assays, tumor volume appears to be the most precise and most relevant predictor of radiotherapy outcome.

The precision requirements for the measurement of tumor volume are small. Statistical considerations show that a precision of $\pm 50\%$ is sufficient for reasonable results.

Conclusion: The data evaluated here clearly suggest that tumor volume is the most precise and most relevant predictor of radiotherapy outcome. Its determination is cheap and easy and with sufficient accuracy achievable in most radiotherapy departments. Individual tumor volume should always be reported in clinical studies and considered in data analyses.

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ORAL

Randomized trial comparing preoperative irradiation versus the use of non-steroidal-antiinflammatory drugs for prevention of heterotopic ossification following prosthetic total hip replacement

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Purpose: In vivo data support the effectiveness of early preoperative irradiation within 4 h before operation in suppressing the development of heterotopic ossification (HTO) after total hip replacement (THR). This procedure can entail logistical difficulties. A randomized trial was undertaken to assess the efficacy of late preoperative irradiation in the evening before the day of operation compared with the use of non-steroidal-antiinflammatory drugs (NSAID).

Methods: Between 1995 and 1996 103 patients with normal risk factors for HTO following elective hip replacement were randomized to receive preoperative irradiation (single 7 Gy fraction) or NSAID (diclofenac-colestyramine). X rays of treated hips were obtained immediately and 6 months after surgery. HTO was scored according to the Brooker grading system. A group of 100 patients, who received no prophylactic therapy after THR between 1988 and 1992, were analysed as untreated historical control group.

Results: The incidence of HTO was 48% in the irradiation-group (Brooker Score I: 52%; II: 36%; III: 5%; IV: 0%), 9.3% in the NSAID-group (Brooker Score I: 7.5%; II: 1.8%; III: 0%; IV: 0%) and 65% in the untreated control group (Brooker Score I: 26%; II: 15%; III: 19%; IV: 5%). Regarding overall HTO there was a significant difference between the two treatment groups. Analysing the clinically significant HTO (Brooker score III or IV) no significant difference was noted between irradiated

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POSTER

Factors determining late complications following postoperative radiotherapy in endometrial carcinoma

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Purpose: Our aim was to evaluate the influence of patient- and treatment-related factors on the risk of late effects of normal tissue (LENT) after postoperative radiotherapy (RT) in endometrial cancer (EC) patients (pts).

Methods: We performed the retrospective analysis of data of 247 EC pts treated with surgery followed by RT including Caesium or Radium brachytherapy (BRT) and external beam RT (XRT). Mean BRT dose rate at 0.5 cm was 0.75 ± 0.49 Gy/h ($0.42-1.9$ Gy/h) and mean BRT dose was 50.1 ± 11.7 Gy at 0.5 cm ($14.5-71.0$ Gy). Mean XRT dose within the target volume was 44.5 ± 3.4 Gy ($20.0-60.0$ Gy) given in fractions of 1.4 to 2.26 Gy (mean 1.82 ± 0.15 Gy). Median follow-up was 7.3 years. Normalised Total Dose (NTD) was calculated based on linear-quadratic equation including XRT and BRT doses. EORTC/RTOG scale with elements of SOMA/LENT table was used to score LENT.

Results: 144 pts experienced LENT, most frequently from rectum (49% pts) and urinary bladder (25% pts). Severe LENT (grade 3 or 4) were observed in 11% of pts. Multivariate Cox test showed that NTD ($p = 0.000$), XRT fraction dose ($p = 0.041$) and BRT dose rate ($p = 0.036$) were independent risk factors for LENT. Prolongation of RT time and box technique were correlated with lower LENT risk, but were not independent factors in multivariate test. No clinical factor (age, parity, prior abdominal surgery, FIGO stage, diabetes, hypertension) was independently associated with LENT.

Conclusion: The risk of LENT depends mainly on treatment-related factors. High rate of LENT in our pts was a basis of modification of RT schedule.

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POSTER

Prognostic impact of reoxygenation in cervical cancers treated with definitive radiotherapy

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Objective: We have investigated the oxygenation status of cervical cancers in patients undergoing definitive radiotherapy.

Materials & Methods: 28 patients with squamous cell carcinoma of the cervix uteri FIGO II/III underwent polarographic measurement of tumor oxygenation with an Eppendorf pO₂-histograph prior to and during definitive radiotherapy (at 20 Gy and at the end of XRT). All received combined external irradiation and HDR-brachytherapy.

Results: We found a broad range of pO₂-values in the 28 patients. Significant hypoxic areas were detectable in one third of the patients. The mean and median pO₂-values did not correlate with tumor stage or tumor volume. 22 patients achieved a complete remission of the primary local tumor. In this subgroup of responders, the median pO₂ at 0 Gy and 20 Gy was higher than in patients with persistent or recurrent disease (at 0 Gy: 22 vs. 16 mmHg, $p < 0.01$; at 20 Gy: 37 vs. 13 mmHg, $p < 0.01$). A pretreatment pO₂ below 10 mmHg, was found in 10/27 patients. In five of them, it persisted at 20 Gy and all failed (four locally, one distant). The other five tumors with a low initial pO₂ showed an increase in the median pO₂ at 20 Gy, and all five were locally controlled although one developed distant disease. In the 17 patients with a pretreatment pO₂ above 10 mmHg, 16 were locally controlled.

Conclusions: An early increase in tumor tissue pO₂ is a favourable prognostic sign suggesting a role of "reoxygenation".

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POSTER

Differentiation patterns of secondary skin fibroblasts from radiotherapy patients with different degrees of radiation-induced skin fibrosis

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Purpose: Radiation-induced terminal differentiation of fibroblasts is an important step in the development of fibrosis after radiotherapy. In a retrospective study of postmastectomy radiotherapy patients we have examined possible relations between the differentiation pattern and the risk of fibrosis in individual patients.

Methods: Quantitative differentiation patterns of fibroblast precursors (mitotic cell types MFI, MFII, MFIII) and functional fibrocytes (PMF) were determined by clonal culture of secondary fibroblasts established from biopsies from the unirradiated upper arm and correlated with the individual risk of fibrosis.

Results: In a pilot series of eight patients, a high risk of fibrosis was associated with an increased ratio of late relative to early mitotic fibroblasts indicating that progression towards later differentiation states may increase the risk of fibrosis.

Conclusion: The present results support the hypothesis that disturbance of the balanced composition of fibroblasts/fibrocytes is a factor in the development of radiation-induced fibrosis and suggests a potential predictive assay for radiation-induced fibrosis. A blind study of 31 patients is in progress.

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POSTER

Malignant pleural mesothelioma (MM): Outcome following radiotherapy in 300 patients

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Background: The incidence of MM continues to increase, particularly in industrial regions. As MM is currently viewed with therapeutic pessimism,

it is important to identify any factors which may correlate with a favourable treatment outcome. The outcome following radiotherapy (RT), either alone or in combination with other modalities, of patients treated at our institute were reviewed.

Methods and Materials: A retrospective review was conducted of the outcome of treatment for 300 patients who were treated at the DDHCC using external RT in the period 1980–95. The patient characteristics studied were: age, sex, performance status, TNM classification, prior treatments, details of radiation scheme, adjuvant treatments, treatment toxicity, response rates and duration, and survival.

Results: The median patient age was 60 yrs (range: 39–82); prior treatments included surgery ($n = 3$), chemotherapy ($n = 27$), and immunotherapy ($n = 9$). The median radiation dose was 37 Gy (8–68 Gy) and median fraction size 4 Gy (1–8 Gy). 14 different schedules were used during this period but 50% were treated using 11 fractions of 4 Gy (3x per week). These variables were subjected to a multivariate analysis.

Detailed results will be presented. It will be discussed how this information can be used to identify patient groups favourable responding to radiotherapy or for trials of combined radiotherapy and hyperthermia, and other experimental therapies, including new chemotherapeutic agents and gene therapy.

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POSTER

Response and cosmesis of two, short duration radiotherapy regimens for epidemic cutaneous Kaposi's sarcoma

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Objectives: To determine optimal radiotherapy for response and cosmesis of HIV related Kaposi' sarcoma.

Methods: 596 lesions in 57 patients were prospectively treated using two radiotherapy regimens, 16 Gy in 4 fractions over 4 days or 8 Gy single fraction. 172 lesions were randomly allocated with the remainder being treated according to the patients preference. A 4 point system was developed to assess response and cosmesis 6 weeks after completion of radiotherapy.

Results: Overall response rate (CR and pCR) 81% (482/596). Lesions treated with 16 Gy/4 F had a response rate of 88% (174/198) and the 8 Gy/1 F 77% (308/398). There was no significant difference according to χ^2 tests ($P > 0.5$). Response duration for both regimens was 19 weeks. Cosmesis of an acceptable quality (0/1) was found in 92% (366/398) of lesions treated with a single fraction and 86% (170/198) of lesions treated with 4 fractions. ($0.1 > P > 0.5$).

Conclusions: Radiotherapy is an effective treatment for localised epidemic KS. A single fraction of 8 Gy provides an acceptable response and cosmesis.

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POSTER

Re-treatment of locally recurrent or persistent nasopharyngeal carcinoma by second course radiotherapy

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Purpose: To assess the outcome and determine the prognostic factors for patients with locally recurrent or persistent nasopharyngeal carcinoma (NPC) treated by second course radiotherapy (RT).

Materials and Methods: From 1978 to 1995, 199 NPC patients who were initially treated in the Department of Radiation Oncology, Chang Gung Memorial Hospital-Linkou, had local failure in the nasopharynx and were re-treated by RT. Seventeen patients whose re-treatment dose was less than 20 Gy were excluded from this study. The time from the initial RT to re-treatment ranged from 2 to 189 months (median: 20 months). All patients were treated by external RT. 25 and 13 patients received brachytherapy and radiosurgery, respectively, as a boost treatment. Since 1993, 35 patients received conformal radiotherapy as their external RT. Re-irradiation dose specified at nasopharyngeal vault ranged from 20 to 67.2 Gy (median 50 Gy), and the cumulative dose ranged from 96.8 to 135 Gy (median 113 Gy). 71 patients received 1 to 8 courses cisplatin-based chemotherapy.

Results: The 1-, 2- and 3- year survival rate was 58%, 32% and 22%, respectively. Patients whose tumor relapsed later than 2 years after first treatment had better survival than those earlier than 2 years, 2-year survival rate was 39% vs. 25% ($p = 0.015$); patients without intracranial invasion by tumor or cranial nerve palsy had better survival than those with, 2-year survival rate was 42% vs. 13% ($p = 0.006$); patients whose re-treatment dose was more than 50 Gy had better survival than those less than

50 Gy, 2-year survival rate was 37% vs. 25% ($p = 0.003$). The use of chemotherapy, brachytherapy, radiosurgery or conformal radiotherapy did not have prognostic significance in this analysis. In 92 patients who were treated by conventional external RT and followed up with CT scan or MRI, 14 were found to develop brain necrosis in the image study, which occurred in 11–32 months (median: 14 month) after re-irradiation. However, no brain necrosis occurred in patients treated by conformal radiotherapy in a follow-up period of 8 to 24 months.

Conclusion: 22% patients with locally recurrent NPC treated can survive more than 3 years by second course RT. The time interval from first treatment to relapse, intracranial invasion/cranial nerve palsy and re-treatment dose had prognostic significance. Higher than 50 Gy radiation dose may be necessary to achieve better survival. From our preliminary data, conformal radiotherapy for these patients may not improve the survival, however, it might decrease the brain necrosis shown by image study.

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POSTER

Conformal radiation therapy for retinoblastoma: Comparison of various 3d proton plans

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Conventional radiation treatment for retinoblastoma can result in potentially severe cosmetic and functional long-term side effects. In the present study, 3 different tumor locations (temporal, central, and nasal) in the retina were assumed and various field approaches were tested to optimize the dose distribution to target and non-target tissues, using the 160 MeV, fixed, horizontal proton beam of the Harvard Cyclotron Laboratory. CT-scans were obtained with 3 different eye positions: straight, temporal, and nasal rotations. Tumor volume, microscopic target and critical structures were drawn and 3-D treatment plans were performed. Different oblique beam arrangements with outward or inward rotation of the eye were compared with the lateral beam orientation with straight eye position. Full coverage of the tumor and microscopic target to total doses of 46 CGE (Cobalt Gray Equivalent) and 40 CGE was obtained. Neither plan delivered significant dose to pituitary gland, contralateral eye, or brain tissue. For all 3 tumor locations (temporal, central, and nasal), isodoses on the treatment plans and dose-volume histograms demonstrated improved dose distribution by using a 45° oblique latero-anterior field. With this arrangement, the lens was almost completely spared: 50% received less than 0.5 CGE. The advantage was most evident for orbital bone and soft tissues. In particular, this technique was able to spare the growth centers located in the medial and lateral aspects of the orbital rim, therefore permitting normal orbital growth.

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POSTER

Dosimetry in vivo in radiotherapy of head and neck cancer patients

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Purpose: The evaluation of quality of head and neck patient irradiation by analysis of entrance and exit doses measurements, calculation of midline doses, dosimetric errors calculation and analysis, and defining their sources.

Methods: The study included 262 patients (300 fields). 1015 entrance and 863 exit doses were measured. 863 midline doses were calculated. 50 measurements were performed using TLD and the remaining by semiconductor diodes.

Results: The mean dosimetric errors of midline, entrance and exit doses were respectively 0.42%, -1.04% and -0.27%. Numerous sources of errors were found and some of them were corrected during the treatment. There were the following most important factors influencing the value of dosimetric error: kind of wedge filters and fixating masks, SSD, tumour and detector localisation, irradiation technique, time of radiotherapy and discrepancies between real and measured thickness of irradiated volume.

Conclusion: The value of dosimetric error is not constant and it may change during long time of fractionated radiation treatment. Some anatomical (tumour localisation, density of surrounding tissues) and technical (irradiation technique, immobilisation masks, wedge filters and the discrepancy between planned and real SSD) parameters of irradiation have to be precisely defined and checked out during the treatment because they can be the main sources of dosimetric errors.