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 ±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.

429 ORAL

Randomized trial comparing preoperative irradiation versus the use of non-steroidal-antiinflammatory drugs for prevention of heterotopic ossification following prothetic 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-colestyramin). X rays of treated hips were obtained immediately and 6 months after surgery. HTO was scored accending 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

430 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.

431 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 pO_2-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 pO_2-values in the 28 patients. Significant hypoxic areas were detectable in one third of the patients. The mean and median pO_2-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 pO_2 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 pO_2 below 10 mm Hg, 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 pO_2 showed an increase in the median pO_2 at 20 Gy, and all five were locally controlled although one developed distant disease. In the 17 patients with a pretreatment pO_2 above 10 mm Hg, 16 were locally controlled.

Conclusions: An early increase in tumor tissue pO_2 is a favourable prognostic sign suggesting a role of "reoxygenation".

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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.

433 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,