MORPHOLOGICAL AND FUNCTIONAL STUDIES OF THE RESPIRATORY MUCOSA AFTER RADIATION THERAPY

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Purpose: Evaluation of radiation damage to the normal nasal respiratory mucosa by micro and ultrastructural studies and assessment of mucociliary clearance with saccharine test.

Methods: Before, at the end, and 6-24 months after radiotherapy (RT), tracheal biopsies were performed in the posterior aspect of the inferior turbinate in 6 patients (pts), 4 males and 2 females, aged 55-73 affected by pharyngeal squamous cell carcinomas. The area of the biopsy was not involved by the tumor but was included in the planning target volume (PTV) for RT. The total dose ranged from 69.0 to 75.9 Gy. Four pts were treated Q1D 2Gy/fr and 2 pts BID 1.15 Gy/fr 5 days/week. The biopptic specimens were fixed in NaCl 0.9% and glutaraldehyde 2.5%, dehydrated in alcohol and included in resin. Two millimeter slices were obtained by ultramicrotome Reichert Suprornica (LW 970201) and observed with optical microscope. Eighty nanometer sections were stained with uranyl acetate and lead citrate and observed with electron microscope.

Results: At the end of RT, we observed structural changes in the epithelium with decreased number of cells. In the choriorn, rarefaction of blood vessels and glands with interstitial sclerosis was evident. The last biopsy showed reconstruction of the normal mucosal pattern with revascularization and reduction of glands. These findings were in agreement with the saccharine functional test. Further observations concerning ultramicroscopic data will be presented.

407 SILICONE TISSUE-EXPANSER PROSTHESIS (STEP) TO PROTECT THE SMALL BOWEL DURING RADIATION THERAPY FOR UTERINE MALIGNANCIES


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Purpose: RT-induced small bowel injury is a dose-limiting factor in gynecological cancers. Therefore, a STEP connected with a subcutaneously located self-sealing valve system was introduced surgically to push small bowel outside the treatment volume.

Methods: Between 1990 and 1995, 41 patients with a diagnosis of cervical (n = 35) and endometrial (n = 6) cancer were treated with curative (n = 29) or palliative (n = 12) RT after undergoing treatment planning simulation with the use of small bowel and contrast medium. All patients underwent surgical placement of a temporary STEP prior to RT. Median age was 48 (28-70) years. Two patients with local relapse and 30 with new diagnosis were treated. According to the FIGO classification, there were 3 stage I, 1 stage II, 6 stage III, and 4 stage IV patients. All patients received external pelvic (n = 38) or pelvic and parametral (n = 2) RT with a median total dose of 54.4 (48-72 Gy) during a median treatment time of 3.7 (2.5-5.3) Gy. Intravenous thromboprophylaxis was given in 36 patients with a median dose of 30 (3-40 Gy). Median AP/PA field size was 250 (164-497) cm² median lateral opposed field; surface was 304 (159-218) cm². Median measured small bowel surface was 6 (0-107) cm² in the AP/PA fields, and 0 (0-20) cm² in the lateral fields.

Results: As of January 1996, the System overall and DFS were 44% and 44%, respectively. Toxicities were graded according to RTOG. During external RT there were 27 patients with GI, 9 with GI, and 5 with G2 gastrointestinal toxicity. During brachytherapy, the same toxicity was GI in 35 patients, and G3 in 6. At the end of the treatment, only 5 patients had G2 gastrointestinal toxicity. No gastrointestinal toxicity was recorded at 3 and 6 months following treatment only. Only 3 patients developed major complications requiring surgery; 2 (one small bowel obstruction and one fistula with abscess) related to STEP and one related to RT at 32 Gy (unrelated lin) resulting with surgical correction, and application of a STEP to complete her treatment.

Conclusion: Placement of a silicone tissue-expander prosthesis is correlated with a low rate of gastrointestinal toxicity due to major reductions of small bowel quantity within the radiation volume without any major surgical toxicity related to its placement.

408 THE INFLUENCE OF DOSE PER FRACTION ON THE PATHOGENESIS OF RADIATION NEPHROPATHY

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PURPOSE: The aim of this study was to determine whether there were different target cells responsible for radiation-induced nephropathy after low dose and high dose per fraction treatment and whether the capacity for repair of damage was influenced by the dose per fraction.

METHODS AND MATERIALS: Both kidneys of male Wistar rats were irradiated with either 10 Gy single dose or 26 Gy with 2 Gy per fraction. Scintillation, Crenatum and blood hematocrit levels were assessed prior to radiotherapy and at intervals of 8 weeks thereafter. Two animals were killed at 4, 8, 16 and 24 weeks. In each group, and both kidneys of each animal were examined by electron microscopy.

RESULTS: In both dose groups, a significant increase in BUN and creatinine levels together with a decrease in hematocrit level was observed at 16 weeks and this was followed by an apparent improvement at 24 weeks. There was no statistical difference in these responses between the two dose groups. The morphological changes in both dose groups were essentially similar, however they differed in severity. At 4 weeks after irradiation, glomerular and proximal tubular injury were observed in both groups. A marked increase of glomerular and tubular injury in the 10 Gy dose group, with no apparent progression in 26 Gy dose group, was detected at 8 weeks. At 16 weeks, a noticeable improvement in both tubular and glomerular lesions, especially in 10 Gy dose group was observed. No apparent difference from 16 weeks of evaluation was found at 24 weeks.

CONCLUSIONS: These findings showed that the morphological changes observed with low doses are the same as with high doses of radiation but differ in degree and both glomerular and tubular changes are visible at the same period of time. There is some recovery in kidney after irradiation, but the extent of recovery process is somewhat limited.

409 ZESLE A LONG-TERM CARDIAC MORTALITY FOLLOWING RADIATION THERAPY FOR HODGKIN'S DISEASE: ANALYSIS WITH THE RELATIVITY SERIALITY MODEL

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Purpose: To assess the increased risk of ischaemic heart disease (IHD) death in the patients treated for Hodgkin's disease with radiation therapy as primary treatment at a single institution. To quantify the dose response of IHD using the relative seriality model of normal tissue complication probability (NTCP) and individual clinical data.

Materials and Methods: A retrospective study analysis of 177 patients diagnosed for Hodgkin's disease between 1972-1985 and who received radiation therapy (RT) as primary treatment at Radiationhems Karolinska Hospital. The general population formed the control group. The individual disease planning and measurement analysis was used on the individual treatment data and simulation film. Individual complication data and individual reconstructed dose volume histograms of the heart were analyzed with the use of the relative seriality model describing NTCP. The maximum of likelihood was used to fit the individual observed complication data. The material was also analyzed grouping the material according to dose volume constraints. The method of chi-square was used for the fit.

Results: Of the 177 patients, 13 (8.4%) died due to heart disease. The Standardized Mortality Ratio (SMR) was 5.6 (95% CL, 2.7 to 8.4) Analysis of dose-volume histograms showed an increasing risk with increasing dose to a larger volume fraction. The relative seriality model could not unambiguously model the individual observed complication data. The group analysis was successful and resulted in the dose response parameters: \( D_{10} = 10 \text{ Gy}, D_{50} = 31 \text{ Gy} \) and \( a = 0.6 \).

Conclusion: A significantly increased risk of dying of ischaemic heart disease death following radiation therapy for Hodgkin's disease was found. The risk was increased with higher dose and larger volume fraction irradiated. The threshold effect of the dose was observed in the material. The heart was found to be less sensitive during irradiation for Hodgkin's disease compared to breast cancer. This may be due to specific sensitive structures in the heart (e.g. left arterial descending coronary artery). Modeling of the individual clinical data proved to be hard, instead the model could describe the group data.

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