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### Computed tomography (CT)-Based treatment planning in prostate cancer

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**Purpose:** CT-information is now widely used in the delineation of the target volume and critical structures for radiotherapy. We have investigated the effect of CT-based treatment planning on field size, field position and acute toxicity in prostate cancer.

**Methods:** Between 1980 en 1995, 361 patients with prostate cancer received curative radiotherapy with an anterior-posterior-bilateral 3-fields technique. Between 1980 en 1988, the size and position of the fields were determined by conventional simulation techniques (group I; n = 70). Between 1989 and 1992, a CT-scan was performed after the simulation to check the size and position of the radiation portals (group II; n = 180). Since 1992, the target volume was only determined by CT-scanning (group III; n = 111).

**Results:** The length of the fields increased significantly with the introduction of CT-based treatment planning (I: 7.0 cm; II: 7.7 cm; III: 8.3 cm;  $p < 0.001$ ). The same was observed for the width of the lateral fields (I: 6.2 cm; II: 8.3 cm; III: 9.1 cm;  $p < 0.001$ ). The width of the anterior posterior field was significantly higher in group III than in the other groups (I: 8.3 cm; II: 8.2 cm; III: 9.2 cm;  $p < 0.001$ ). The expansion of the field size was mainly in cranial and dorsal direction, to cover the seminal vesicles. There was no increase in acute toxicity of bowel and urinary bladder.

**Conclusion:** The introduction of CT-planning has resulted in larger treatment portals, to cover the whole target volume. This has not resulted in a significant increasing toxicity. The use of conformal therapy may further enable us to increase the dose leading to improved cure rates with acceptable toxicity.

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### Radiotherapy for oesophagus carcinoma: The impact of p53 on treatment outcome

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**Background and Purpose:** P53 is mutated in many human tumours. Its role is known in the cellular response to ionizing radiation and other DNA damaging agents. We evaluated the predictive value of p53 protein status determined by immunohistochemistry (IHC) in patients treated with radiotherapy alone, for carcinoma of the oesophagus.

**Material and Methods:** IHC for p53 protein was performed on paraffin-embedded specimens from 69 patients with adenocarcinoma and squamous cell carcinoma of the oesophagus. All patients were treated by external beam irradiation combined with intraluminal brachytherapy.

**Results:** 54% (37/69) of the tumours showed overexpression of the p53 protein. No correlation with pretreatment parameters for p53-positive and p53-negative cases was detected. Overall survival as well as distant metastases free survival was superior for p53 negative tumours. Local recurrence was slightly better in the p53 negative group, but this was dose dependent.

**Conclusions:** Mutated p53 protein in oesophagus carcinoma, as determined by IHC, was an independent prognostic factor in this group of patients.

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### Clearance of lymphadenopathy in epidermoid carcinomas treated by radiotherapy (RT)

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**Purpose:** To determine the patterns of clearance of lymphadenopathy following RT, which have been used shortly after RT as a potential predictor of nodal control.

**Materials and Methods:** Sequential computed tomographic (CT) scans of 18 uterine cervix cancer patients and 60 head and neck cancer patients with radiologically-metastatic lymph nodes (LNs) treated by definitive RT or preoperative RT (50-70 Gy) were evaluated. A total of 136 LNs identified on pre-RT and post-RT CT scans were used: cervix (n = 26), epipharynx

(n = 31), hypopharynx (n = 31), larynx (n = 21), oropharynx (n = 15), and oral cavity (n = 12). The daily volume decrease (DD) in the observation period ( $46.7 \pm 10.7$  days) was estimated to determine its relationship with the initial LN size. Neck LNs resected after RT were histologically reviewed.

**Results:** Volume clearance of greater than 50% was obtained for 104 LNs (76.5%). The DD significantly correlated with the LN diameter (D) with an exponential equation,  $DD = a \cdot D^b$ ; the exponent b was 2.97 for the entire group, ranging from 2.32 (cervix) to 3.42 (oral cavity). The capacity of clearance (DD/LN volume) was larger for the epipharynx group than the others. Treated LNs histologically consisted of necrosis, fibrous tissues, lymphatic tissues, and few cancer cells if any.

**Conclusions:** The exponent b being smaller than 3.0 suggests that the larger the LN volume ( $\pi D^3/6$ ), the longer the time to achieve a complete response. Also, the capacity of clearance will be a function not only of the radiosensitivity of tumor cells but also of the quantity of non-cancer cell components of LNs.

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### In-vitro radiosensitivity of lymphocytes and clinical radiation reaction

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**Background:** We have investigated the in-vitro radiosensitivity of peripheral blood lymphocytes with a special FISH/CISS-technique in radiotherapy patients.

**Materials and Methods:** A total number of 41 cancer patients (23 prior to and 18 after radiotherapy) plus three AT-homozygotes were investigated. For to estimate the intrinsic radiosensitivity, blood samples were taken and irradiated in vitro with 0 (control) or 0.7 or 2 Gy, standard 48 h-lymphocyte cultures were prepared, chromosomes #1, #2 and #4 were simultaneously labelled with a FISH/CISS-technique and metaphase spreads were scored for radiation-induced chromosomal breaks.

**Results:** The maximum acute and/or late normal tissue radiation reaction in the 41 radiotherapy patients was grade 0 in 10, mild (grade 1) in 20 and moderate (grade 2) in 8. Three patients showed above-average (grade 3, n = 2) or extreme (grade 4, n = 1) normal tissue reactions. The number of radiation-induced breaks induced after in-vitro irradiation was significantly higher in lymphocytes of patients who showed a severe or extreme radiation reaction as compared to patients with no or mild to moderate normal tissue reaction:  $0.105 \pm 0.062$  in patients with no radiation reaction,  $0.084 \pm 0.051$  for grade 1,  $0.097 \pm 0.037$  for grade 2,  $0.320 \pm 0.209$  for grade 3-4 and  $0.550 \pm 0.243$  in AT-homozygotes. The difference between patients with grade 0 versus grade 1 or grade 2 normal tissue reaction was not significant.

**Conclusions:** The radiosensitivity of lymphocytes in patients with severe clinical radiation reactions was in the range between normal radiosensitivity and the radiosensitivity of AT-homozygotes. Detection of patients with enhanced intrinsic radiosensitivity might be possible with this method.

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### Tumor tissue pO<sub>2</sub>, S-phase-fraction, p53-status and response to radiotherapy in cervical cancers

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**Objective:** We have investigated the prognostic impact of proliferation, p53-status and oxygenation in patients with cervical cancers undergoing definitive radiotherapy.

**Materials & Methods:** 37 patients with squamous cell carcinoma of the cervix uteri FIGO II/III who were treated with curative intent underwent polarographic measurement of tumor oxygenation with an Eppendorf pO<sub>2</sub>-histograph prior radiotherapy. All received combined external irradiation and HDR-brachytherapy. Tumor specimens were examined immunohistologically for p53- and MIB-expression and S-phase-fraction was measured by flow cytometry.

**Results:** 27/37 patients achieved a clinical CR 3 months after treatment. The only significant prognosticator was the initial median tumor tissue pO<sub>2</sub>

	N	median pO <sub>2</sub> (mm Hg)	S-phase (%)	p53-pos.
Clinical CR	27	26.4 ± 19.7	11.9 ± 7.1	14.5 ± 25.9
No CR	10	11.4 ± 10.5	16.3 ± 6.2	10.6 ± 13.2
		p ≤ 0.05	n.s.	n.s.