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POSTER

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 ± 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 ± 0.062 in patients with no radiation reaction, 0.084 ± 0.051 for grade 1, 0.097 ± 0.037 for grade 2, 0.320 ± 0.209 for grade 3-4 and 0.550 ± 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 pO₂, 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 pO₂-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 pO₂

	N	median pO ₂ (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.

* indicates Poster Discussion

(table 1). There was, however, a significant negative correlation between S-phase-fraction and pO₂.

Conclusions: Fast proliferating tumors have a lower pO₂. However, the initial pO₂ seems to be the strongest predictor for response to radiotherapy in cervical cancers.

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Functional and structural immunodefects after limited volume radiotherapy

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Purpose: The effect of limited volume irradiation on the function of the human immunosystem has not been well documented. In a prospective study structural and functional aspects of the immunosystem were analyzed in 15 patients receiving a 26 Gy course of periaortic irradiation for stage I testicular seminoma

Methods: Immunophenotyping of peripheral lymphocytes (CD3, CD4, CD8; CD19, CD45RA, CD45RO, CD45RA, CD56, CD25, HLA-DR, CD34), lymphocyte transformation test (LTT) with mitogens (PHA, Con A, OKT3, Leu4, PWM) LTT with antigens (tuberculin, mumps, measles, rubella, varizella, HSV, influenza A, CMV, tetanus, candida, diphtheria) was performed at 0 Gy, 14 Gy and 26 Gy as well as 6 and 16 weeks after RT.

Results: All lymphocyte populations are reduced during and after radiotherapy. CD 19 pos. B-lymphocytes and CD45RA positive naive cells are most sensitive. NK are more resistant. No significant alterations in lymphocyte reactivity towards mitogens and antigens was seen.

Conclusion: Although RT leads to an significant reduction in peripheral lymphocyte counts no functional impairments could be detected. Furthermore, most lymphocyte subsets recover to low normal levels 16 weeks after RT.

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Low dose irradiation for macular degeneration

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Aim: To determine the response of macular degeneration to low dose external beam irradiation and the acute and late morbidity on the eye.

Methods: Forty-seven patients (49 eyes) meeting stringent ophthalmological criteria underwent low dose irradiation delivered with a 6 MV linear accelerator to 1600 cGy in 8 equal fractions through an ipsilateral anterior oblique field angled 7°–10° posteriorly from June to December 1996. Ophthalmological evaluation was accomplished at 1, 3, 6, 9 and 12 months later.

Results: There was no acute or late toxicity. Visual acuity stabilized for most patients. Subjectively, 9 reported improvement and 4 slight worsening of vision but this did not always agree with objective acuity measurements. Edema and hemorrhage decreased or disappeared in the majority, with only 1 patient showing new areas of hemorrhage.

Conclusion: 1600 cGy causes regression of hemorrhage and edema, with stabilization of vision and without toxicity in the majority of patients. The results of a detailed ophthalmological review in progress will be presented.

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Current practice in early breast cancer post-operative irradiation: An Italian survey

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Purpose: To evaluate the present radiotherapy (XRT) management of early breast cancer (EBC), a questionnaire on adopted radiation parameters was sent to all XRT Departments of Northern Italy. This survey is also aimed at helping in the definition of national guidelines for the EBC post-operative XRT.

Methods: 50 XRT Departments received a questionnaire on specific aspects related to pre-treatment evaluation, treatment prescription, treatment preparation and execution for whole breast and tumor bed XRT, surgery-radiation-chemotherapy combination and follow-up. Analysis of variables and comparison with the European standards were performed.

Results: 37 out of 50 (74%) questionnaires, regarding ~5,500 patients treated per year, returned. A general agreement between Departments was found on main XRT aspects (total dose delivered to whole breast, basic XRT technique, beam modifiers, patient position, acute and late toxicity recording, etc.). Data dispersion was mainly noted on simulation and treatment planning procedures and quality of boost irradiation.

Conclusions: This survey evaluates the current practice of irradiation for EBC in Northern Italy. Results are generally in agreement with the European standard of reference (EORTC-EUSOMA Consensus document, 1991). However, several parameters need to be standardized and all these information represent the background to define national guidelines adapted to the Italian situation and resources.

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Locally advanced and metastatic thyroid cancer – 15-year results of adjuvant or palliative external beam radiotherapy

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Purpose: The role of postoperative external radiotherapy (RT) for thyroid cancer is still controversially discussed. We have analyzed long-term local control, systemic response and prognostic factors in patients with locally advanced, recurrent or metastatic disease.

Methods: Between 1976–1992, 121 out of 483 consecutive patients (46 m., 75 f.) with histologically proven thyroid carcinoma (papillary, n = 31; follicular = 40; medullary = 21; undifferentiated/anaplastic = 24; and other tumors = 5) received RT and were followed for a median of 7.5 years. Prior therapy was surgery (92) and radio-iodine therapy (63). The RT was indicated for advanced papillary/follicular T4N+ tumors, macroscopic tumor burden after resection and unfavourable histologies. All cases were stratified into 3 groups according to tumor burden prior to RT: R1 resection of primary tumor (n = 33); R2 resection or locally recurrent tumor (46), or metastatic tumor burden (42). RT was applied to tumor and lymphatics or metastatic site with 2 Gy single dose up to 40–60 Gy total dose.

Results: Complete (CR) and overall response (CR/PR) was 100% and 100% respectively in group 1, 61%/55% in group 2, 33%/17% in group 3. In the latter groups, relief of tumor-associated symptoms was achieved in 68% (group 2) and 58% (group 3). Treatment toxicity WHO 2°/3° occurred in 5%. In long-term analysis, loco-regional progression or relapse occurred in 18% (group 1), 46% (group 2) and 83% (group 3) (p < 0.001). The 5- and 10-year disease-free-survival rates were 83% and 78% respectively for group 1, 48% and 42% (group 2) and 24% and 15% (group 3) (p < 0.05). In univariate analysis, tumor burden, initial CR, histology (papillary and follicular) and gender were positively correlated with long-term relapse- and disease-free survival. Even patients with metastatic disease achieved long-term survival when initially presenting with a single metastatic site.

Conclusion: Postoperative RT is effective in managing locally advanced thyroid cancer.

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Radiotherapy with carbogen breathing and nicotinamide in locally advanced non-small cell lung cancer (NSCLC)

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Purpose: Combining radiotherapy (XRT) with carbogen (C) and nicotinamide (NAM) has been proposed as a strategy to overcome acute and chronic hypoxia. The feasibility, toxicity and influence on local control of this treatment was tested in locally advanced, non-small cell lung cancer patients (pts).

Methods: Between January 1996–June 1996, 38 pts were randomised: 21 pts to radiotherapy alone (XRT) and 17 pts to radiotherapy + carbogen + nicotinamide arm (XRT + C-NAM). All patients received XRT with fractionation scheme in daily fractions of 3.2 Gy, five days/week up to 14 fraction in XRT arm and 12 fraction in XRT + C-NAM arm. Thus, Biological Equivalent Doses (BED) were reduced by %9 for normal lung tissue and %23 for medulla spinalis in XRT + C-NAM arm.

Results: In general, C-NAM was well tolerated. There was no difference between two arms regarding grade III–IV acute toxicities (p = 0.475). In