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Changes in prostate volume during permanent brachytherapy with JOD 125 and influence on dose distribution (D 90)

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Background: An increase of the prostate volume during permanent brachytherapy may lead to a clinical relevant dose reduction. The time course and the predominant axis of the volume aberration after seed implantation were determined.

Materials and methods: In 96 patients a CT scan before implantation was compared with examinations taken one day, four and eight weeks after implantion. Computer tomography was performed with a Picker 5000 using 3/3 mm slices. Prostate volume and extension in anterior/posterior, lateral and longitudinal axis was recorded with an AqSim/VoxelQ® workstation. The D 90 values were computed using the Prowess® - planning software.

Results: Following an initial increase of all axes, predominant on the a-p direction, there was a continuous decrease, particularly in the lateral dimension:

Extension	CT 1 (pre)	CT 2 (day 1)	CT 3 (week 4)	CT 4 (week 8)
Ant. / Post. (mm)	38,2	42,2 (+11,5%)	39,4 (+2,9%)	36,9 (- 4,2%)
Lateral (mm)	47,4	49,7 (+ 4,8%)	46,5 (- 2,1%)	43,8 (- 7,2%)
Longit. (mm)	30,5	33,1 (+ 7,5%)	33,0 (+ 7,9%)	32,2 (+ 5,3%)
Volume (ccm)	33,1	37,4 (+13,2%)	32,0 (-3,3%)	28,3 (-11,5%)

Where as the a-p. and lateral extension showed a continuous decrease and sunk below the initial datas, the cranio-caudad extension remained nearly unchanged at least during the first eight weeks. Compared with the initially calculated D 90, this effect resulted in a relative increase of the D 90 (132,8 Gy day 1; 142,4 Gy week 4; 152,5 Gy week 8).

Conclusion: The cranio-caudad volume extension showed the smallest decrease compared with the other spatial axis.

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Effects of 5 alpha reductase inhibitors on prostatic carcinoma cells grown in primary culture

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Background: 5 alpha reductase (5α R) plays a key role in the transformation of testosterone (T) in the more active 5α dihydrotestosterone (DHT). In prostate gland both type I (5α R1) and type II (5α R 2) isozymes are expressed. We tested the effectiveness of two 5α R inhibitors (Finasteride, or MK 906, as specific inhibitor of 5α R2 and MK386, a specific inhibitor of 5α R1) in inhibiting cell proliferation of human PCa cells in primary coltures from prostatic biopsies of different pathologies.

Materials and Methods: We analyzed primary cultures derived from 30 cases of Prostatic carcinoma (PCa), 6 cases of high grade PIN and 6 cases of Benign Prostatic Hyperplasia (BPH). Cultures were analyzed for the presence of Prostatic Specific Antigen (PSA), Androgen Receptor (AR) expression and stromal cell contamination by immunocytochemistry. Androgen dependent cell growth was also analyzed. MK906 and MK386 were kindly provided by Merck Sharp and Dohme.

Results: Both 5α R inhibitors are able to reduce significantly and dose-dependently cell proliferation in prostatic primary cultures inducing a significant increase in apoptotic cell number. IC50 values from MK906 were lower when compared to those observed from MK386 whereas the combination of both inhibitors does not increase their overall effectiveness. Primary cell cultures contained about 30% of stromal contamination. Stromal cell presence was essential for prostatic epithelium proliferation. This can also explain the higher effectiveness of MK906 respect to MK386. In fact, 5α R1 (responsible primarily for androgenic catabolism) is mostly expressed in epithelial cells whereas 5α R2 (responsible for DHT local synthesis and release) is expressed in the stroma compartment,. which provides several paracrine factors and DHT itself to epithelial cells. In addition, the effectiveness of MK386 in primary cultures can be explaned considering that the catabolic products (3α and 3β ADIOLs) generated from DHT by 17β hydroxylases modulates prostatic cell growth. Then the inhibition of 5α R1 can alter the catabolism of DHT generating also high levels of β -estradiol having different proliferative effects in prostatic epithelium.

Conclusions: 5α R inhibitors may have an important role in the inhibition of prostatic cancer proliferation as demonstrated by the effectiveness on both human cell lines and PCa primary cultures. In our experience, data concerning the combination effects with other antiproliferative drugs deserve particular attention and will be presented in the near future for an optimal control of PCa.

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The effect of pelvic lymph node irradiation in salvage therapy for prostate cancer patients with a biochemical relapse following radical prostatectomy

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Purpose: Radiation therapy (RT) as salvage treatment for a biochemical relapse (BCR)following prostatectomy has been controversial, but shown to be of benefit with regards to PSA control. However, the appropriate target volume for RT is not well defined. Here, we compare the results of postoperative RT given to an extended field (EF, prostatic fossa and pelvic lymph nodes encompassing at the least the obturator lymph nodes) or to a limited field (LF, prostatic fossa only) as treatment for those with a post-prostatectomy BCR.

Methods: Between 1987-1999, 68 patients were referred for post-prostatectomy RT for a BCR (defined as 2-3 consecutive rises in PSA following prostatectomy). Of them, 46 were treated with RT alone, with 21 patients treated to a EF and 25 patients were treated to an LF. All patients were treated by four-field technique with simulation films verified for EF and LF coverage. The mean field sizes measured 15 x 14 x 12cm and 10 x 10 x 10 cm for the EF and LF, respectively. The mean doses for the EF and LF were 6300 and 6200 cGy, respectively. After 45 Gy, the field for the EF group was shrunk to cover the prostatic bed only.

Results: The ten year actuarial biochemical disease-free survival rates for the EF and LF were 52% and 47%, respectively (p=0.52). The distant metastasis-free survival (DMFS) was 77% and 78% (p=0.93) and overall survival (OS) was 88% and 68% (p=0.61) for the EF and LF group, respectively. A subset analysis of patients with adverse pathologic histopathologic features on surgery (i.e., positive surgical margins, lymph node involvement, seminal vesicle involvement, extracapsular invasion, or perineural invasion) showed a biochemical disease-free survival of 57% and 44% (p=0.22) for the EF and LF group respectively. The DMFS was 84% and 72% (p=0.93) and OS was 92% and 61% (p=0.37) for the EF and LF group, respectively.

Conclusions: For patients with rising PSA levels after a radical prostatectomy, salvage irradiation is a viable option for biochemical control. Our results suggest that EF radiation with coverage of pelvic lymphatics, shows a trend towards PSA control in those with adverse pathologic features, although statistical significance was not achieved. However, a potential prospective study comparing field sizes could more definitively answer our questions as to how to optimize therapeutic options in the postoperative recurrence setting.

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Expression of bcl-2 and p53 as biomarkers in imprint smears of prostate carcinomas and their prognostic value

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Background: The tumour suppressor gene p53 and the proto-oncogene bcl-2 have been shown to be prognostic biomarkers of cancer recurrence in patients with malignant diseases. The aim of this study, was to evaluate the prognostic significance of the expression of p53 and bcl-2 in smears of prostate adenocarcinomas and the results to compare with other prognostic factors.

Material and Methods: Imprint smear samples obtained from 70 patients immediately after radical prostatectomy for prostatic adenocarcinomas were studied. An immunocytochemical stain was performed using anti bcl-2 and anti-p53 monoclonal proteins. The expression of these proteins was related to the Gleason score, tumour differentiation, stage and PSA levels.

Results: Positive expression for p53 and bcl-2 was observed in 50 (71.4%) and 38 (52.8%) smears, of 70 studied tumours, respectively. Our findings demonstrate that p53 and bcl-2 biomarkers in prostatic adenocarcinoma smears, correlated significantly with the degree of Gleason score ($p<0.001$ for p53 and p:0,005 for bcl-2). When combining p53 and bcl-2 positivity with tumour differentiation there was a significant association between these parameters ($p<0.001$). Overexpression of p53 and bcl-