chemotherapy efficacy probably explains the improvement in 1- and 2-year relative survival in patients under 75 with advanced tumours.

Genitourinary cancer

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PSA doubling time (PSADT) is quite variable in untreated, clinically localized, low to intermediate grade, prostate adenocarcinoma (CA)

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Introduction and Objectives: PSADT may allow for a clinician to formulate an individualized management according to the biological behavior of malignancy, as it reflects tumor kinetics. PSADT of untreated, low to intermediate grade, clinically localized prostate CA is analyzed and correlated with clinical parameters.

Methods: A prospective single-arm cohort study has been in progress since November 1995 to assess the feasibility of a watchful observation protocol with selective delayed intervention using clinical, histologic, or rapid PSA progression as treatment indication in clinically localized, low to intermediate grade, prostate CA. Study patients were initially managed with watchful observation alone. Eligible subjects had clinical stage $T_{1b\text{-}2b}N_0M_0$!, Gleason score (GS) $\leq$ 7, and PSA $\leq$ 15 ng/ml. Patients were followed every 3 months for the first 2 years and then every 6 months. At each visit, PSA, medical history and physical examination were obtained. PSADT was estimated from a linear regression of ln(PSA) on time, assuming a simple exponential growth model. Associations of PSADT with baseline clinical parameters were evaluated with correlation analysis.

Results: The study was closed in September 2001 and accrued 244 eligible patients. Of these, 231 patients had at least 3 PSA measurements and a minimum of 6 months follow-up as of March 2003, and were the basis for the analysis of PSADT. Median age was 71 years (range: 49-84). The distribution of clinical stage, PSA at entry and GS were as followed: T1: T2 = 154:77, initial PSA < 5: 5-9.9:10-14.9 = 68:123:40, GS 3-5:6:7:Gx = 49:130:50:2. Median PSA at entry was 6.5 (range: 0.3-14.6). In this cohort, median follow-up was 45 months (range: 6-85) and median frequency of PSA measurement was 8 times (range: 3-21). The distribution of PSADT was as followed: <2 years: 26, 2-3 years: 26, 3-4 years: 26, 4-5 years: 13, 5-10 years: 42, 10-20 years: 26, 20-50 years: 16, >50 years: 56. The median PSADT was 7.0 years. 98 patients (42%) had PSADT > 10 years. PSADT was correlated with clinical T stage (p=0.044), but not with age, GS, or initial PSA level.

Conclusions: PSADT of untreated, low to intermediate grade, clinically localized prostate CA varied widely. 42% of the cohort had PSADT >10 years. PSADT was correlated with clinical T stage.

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Local dose escalation using temporary interstitial source brachytherapy (high-dose-rate) for clinically localized prostate cancer: Long-term outcome in hormone naïve men

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Purpose: To report the long-term outcome of patients treated with high local doses to the prostate in hormone naïve men.

Materials & Methods: A total of 579 men were consecutively treated with EBRT and dose-escalating high-dose-rate brachytherapy (HDR-BT) boost since 1986 in two prospective trials. There were 378 patients treated at William Beaumont Hospital and 201 patients at Kiel University. A short course of neo-adjuvant/concurrent androgen deprivation therapy (ADT) was given to 222 patients. All hormone naïve patients with a follow-up longer than 18 months were selected for this analysis. This cohort of 324 patients was analyzed according to biochemical control (BC), cancer-specific survival (CSS), overall survival (OS), and clinical local recurrence (c-LR) rates. The ASTRO definition for biochemical failure was used.

Results: Mean follow-up for all patients was 5.3 years (1.5-13.9). For all 324 hormone naïve patients, the 5 yr biochemical control (BC) rate was 79%. Cancer-specific survival (CSS) was 98%, and overall survival (OS) was 90%, respectively. The 5 yr clinical local recurrence (c-LR) rate was 7.6%. For patients with one of following poor prognostic factors, $\geq$ T2b, GS $\geq$ 7, initial PSA $\geq$10 ng/ml, the BC, CSS, OS and c-LR 5 yr rates were 81%, 97%, 90% and 4.9%, respectively. For patients with two poor prognostic factors the BC, CSS, OS and c-LR 5 yr rates were 85%, 100%, 91% and 5.2%, respectively. For very high risk patients with all three poor prognostic factors the BC, CSS, OS and c-LR 5 yr rates were 69%, 96%, 87% and 13.8%, respectively.

Conclusions: The results prove that our technique of TRUS guided interstitial conformal HDR-BT is a very successful method to deliver high doses to the prostate. Long-term survival outcomes are excellent in all patients with prostate cancer even for those at highest risk.

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High dose radiation therapy with intensity modulated radiation therapy (IMRT) improves outcomes in localized prostate cancer. A large single institution experience

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Purpose: To compare the outcomes of high dose radiation therapy using IMRT with standard doses using 3D conformal technique in localized prostate cancer at the Cleveland Clinic Foundation.

Materials and Method: A total of 731 patients with localized prostate cancer were treated with conformal external beam radiation therapy between 1992 and 2001. All cases had available pretreatment PSA (iPSA) and biopsy Gleason scores (bGS), no nodal metastasis, a minimum 2 year follow-up, and >5 follow-up PSA levels. AD for $\leq$6 months (AD) was utilized in 47% (8% had AD for >6 months but < 12 months). The frequency by T-stage was: T1-T2A in 75%, T2B-T2C in 17%, and T3 in 8%. The frequency by iPSA was: $\leq$10 in 57% and >10 - 20 in 27%and >20 in 16%. The frequency by bGS was: $\leq$6 in 52%, and > or =7 in 48%. The age range for the patients was from 47 to 85 years (median 68 years). The median follow-up was 45 months (range: 24-103 months). Three-dimensional conformal radiation therapy (3DCRT) was utilized in 453 (62%) patients and IMRT in 278 (38%) patients. The median doses delivered with 3DCRT was 78Gy (range 66 to 78) and IMRT 83Gy (delivered at 2.5Gy per fraction to 70 Gy; this being equivalent to 83 Gy at standard fractionation of 1.8 Gy using an alpha/beta of 2). The ASTRO definition for biochemical failure was used. Toxicity was assessed using Radiation Therapy Oncology Group (RTOG)criteria.

Results: The biochemical relapse free survival (bRFS) for the entire cohort at three years was 85%. The 3-year bRFS for patients treated with 3DCRT was 81% vs. 91% for IMRT (p= 0.0012). A multivariate analysis of factors affecting bRFS was performed for using the following: race, iPSA (continuous), bGS (<or= 6 vs >or= 7), stage (T1-T2A vs T2B-C vs T3), treatment modality (3DCRT vs IMRT), use of AD, and total dose (continuous). T stage (p<0.0001), iPSA levels (p<0.0010), bGS(p=0.0020), and dose (p=0.0508) were independent predictors of outcome. Any (grade 1 or higher) **acute** genito-urinary (GU) side effects for patients receiving 3DCRT and IMRT were 80% and 79% respectively. Grade 2 or higher acute GU toxicity was seen in 20% and 18% of 3DCRT and IMRT patients, respectively. Any (grade 1 or higher) acute gastro-intestinal (GI) side effects for patients receiving 3DCRT and IMRT were 76% and 65% respectively. Grade 2 or higher acute GI toxicity was seen in 19% and 11% of 3DCRT and IMRT patients, respectively. Any (grade 1 or higher) *late* GU side effects for patients receiving 3DCRT and IMRT were 6% and 3% respectively. Grade 2 or higher late GU toxicity was seen in 4% and 1.5% of 3DCRT and IMRT patients, respectively. Any (grade 1 or higher) late GI side effects for patients receiving 3DCRT and IMRT were 15% and 13% respectively. Grade 2 or higher late GI toxicity was seen in 8% and 5% of 3DCRT and IMRT patients, respectively.

Conclusions: Higher doses of radiation delivered by IMRT resulted in better bRFS outcomes in patients with localized prostate cancer receiving external beam radiation therapy using conformal techniques. IMRT can be effectively used to safely increase dose delivery without compromising on quality of life. Hypofractionation is an effective method to dose escalate in localized prostate cancer. Longer follow-up is needed to further substantiate these results.