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BED is not a significant factor for biological recurrence after prostate brachytherapy in Japanese patients

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Purpose/Objective: To analyze long-term outcome for Biochemical recurrence (BCR) after prostate brachytherapy (PPB) in Japanese patients.
Materials and Methods: Between October 2003 and March 2010, 604 consecutive patients with clinically localized prostate cancer (PCa) were treated with PPB in Jikei University Hospital. Median follow-up was 48 months. Among 604 patients, 260 patients (43%) were treated with neoadjuvant, 45 (7.6%) were treated with adjuvant hormone therapy (HT) and 75 (12.4%) were treated with supplemental external radiation therapy (EBRT). BCR was defined as nadir PSA +2ng/ml, using the Phoenix definition. Toxicity was reported according to CTCAE v4.0.
Results: Of the 604 patients, 219 (34.6%) were low-risk, 361(59.8%) were intermediate-risk and 24 (4.0%) were high-risk. The median BED for all patients was 174.4Gy2. At 8 years, BCR-free survival, cancer specific survival and overall survival was 82.2%, 100% and 95.6%, respectively. BCR-free survival at 8 years was 89.9%, 79.4%and 52.5%, for low-, intermediate-, and high-risk group, respectively. BCR-freesurvival of high-risk group was significantly lower than that of low- and intermediate-risk group (p<0.001). BCR-free survival by BED dose was not significantly different. In the multivariate analysis, younger age (p=0.045), higher PSA (p=0.004), higher Gleason score (p=0.006), higher clinical T stage (0.008), disuse of HT(p=0.0021) and disuse of EBRT (p=0.010) were significant variables associated with BCR. Only 3 patients had G3 genitourinary or gastrointestinal toxicity.
Conclusions: PPB results in excellent oncological outcome and tolerable toxicity in Japanese patients. BED was not a significant predictive factor for BCR in this cohort.

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Salvage iodine-125 brachytherapy for local prostate cancer recurrence after radiotherapy

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Purpose/Objective: Retrospectively to analyze short and intermediate-term outcomes and toxicity after salvage BT with I125 for local failure after BT or EBRT for prostate cancer.
Materials and Methods: Between January´10 and September´12, 16 patients with PSA relapse (Phoenix definition for those with previous AD and ASTRO definition for the rest), after histological confirmation with template-guided biopsy, underwent salvage BT with I125 at least 2 years ago from initial treatment (8 BT and 8 EBRT). At relapse, average age was 71 years-old (58-82), median Gleason was 7 (not determinated-9) and PSA pre-salvage BT 5.65 ng/ml (2.81-11.7). Two patients were treated with AD previously salvage BT. The median dose to 90% of prostate volume was 129.1 Gy (84.18-151.47) with a median seed activity of 0.506 mCi (0.319-0.518). Constraint doses for urethra and rectum were 162 Gy and 120 Gy respectively. Toxicities were graded using CTCv4.0.
Results: With a median follow up was 13.5 months (2-32), 11 (68%) patients are freedom from biochemical failure. 5 patients have developed PSA relapse (2 with distant failure evidence and 2 within the first 6 months). There were one Grade 3 toxicity (TURP after acute urine retention) and two Grade 2 toxicities (acute rectal mucositis and acute cystitis in the same patient).
Conclusions: Despite of the short follow-up in some patients, BT is a safe and effective treatment option for salvage treatment, but careful patient selection is essential to improve outcomes.

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Outcomes following brachytherapy for intermediate risk prostate

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Purpose/Objective: The optimal protocol for low dose rate brachytherapy (LDR) in intermediate-risk prostate cancer patients remains controversial. We evaluated our retrospective, single institution experience LDR with short term androgen deprivation therapy(sADT) (protocol-Intermediate risk group: Protocol IRG).
Materials and Methods: From April 2005 to November 2012, 440 patients underwent PPB with I-125. We assessed consecutive 285 patients, treated with LDR without supplemental external beam radiation therapy, including low risk patients (LRG); 147 patients and Protocol-IRG; 139 patients. Prostate specific antigen (PSA) failure was defined as nadir plus 2 ng/m, and benign PSA bounce was also assessed in men with PSA failure. For the evaluation of treatment-related morbidity, we used CTCAE ver.4.
Results: Median follow up length (Protocol IRG vs. LRG) was53 months vs. 55 months, respectively. Pretreatment PSA value was 9.4 ± 4.4 vs6.4 ± 1.6 (p< 0.05). For Protocol IRG and LRG patients, actuarial 5-year overall survival; 97.6% vs. 99.2%; causespecific survival, 100%vs. 100%; distant metastasis-free survival were 100%vs.100%; 5-year bNED (not including PSA bounce) was 99.3% vs. 100%. Acute GU toxicity above grade 2 was seen in 2% ofpatients (1% vs. 1%). Late GU toxicity above grade 3 was seen in 1 patient (LRGpatient) who underwent TURP. Late GI toxicity of grade 2 with rectal hemorrhageoccurred in 1.4% (0.7% vs. 0.7%), which were successfully treated by steroidenema.
Conclusions: Protocol IRG might be a good protocol for intermediate-risk patients which demonstrates good outcome and less morbidity as for low risk patients.

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Clinical and dosimetric analyses of late rectal toxicity associated with HDR brachytherapy for prostate cancer

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Purpose/Objective: Several investigations have revealed that the alpha/beta ratio for prostate cancer is atypically low, and that hypofractionated radiotherapy or high-dose-rate brachytherapy (HDR-BT) regimens using appropriate radiation doses are expected to improve the local control rate for localized prostate cancer. However, the increase in the total biological effective dose (BED) may cause an increase in the severity and incidence of normal tissue complications. The purpose of this study was to investigate if the clinical and dosimetric factors affected the incidence of rectal toxicity after HDR-BT combined with external beam radiotherapy (EBRT).
Materials and Methods: The records of 186 patients with localized prostate cancer treated by HDR-BT combined with EBRT between November 2004 and December 2010 were analyzed. The fractionation schema for HDR-BT and EBRT was prospectively changed. The distribution of the fractionation schema used in the patients was as follows: 9 Gy x 2 + 2 Gy x 20 ($BED_{1.5}$ = 219 Gy, BED_3 = 139 Gy) in 57patients (Group 1); and 9 Gy x 2 + 3 Gy x 13 ($BED_{1.5}$ = 243 Gy, BED_3= 150 Gy) in 129 patients (Group 2). The median follow-up duration was 54 months (range 23 – 96 months). The toxicities were graded based on the National Cancer Institute-Common Terminology Criteria for Adverse Events v3.0. The clinical and dosimetric factors affecting the incidence of Grade 2 or worse late rectal toxicity were analyzed by statistical analyses.
Results: Twenty (10.8%) and one patients developed Grade 2 rectal bleeding and Grade 3 rectal ulcer, respectively. There were no significant differences between Group 1 and Group 2 in the incidence of rectal toxicity (12.3% and 10.9%, respectively). There was no statistically-significant correlation between the incidence of Grade 2 and 3 rectal toxicity and BED escalation. Grade 2 and 3 rectal toxicity occurred in 7 out of 36 (19.4 %) patients receiving the antiplatelet therapy, while it occurred in 14 out of 141 (9.9%) patients without a history of antiplatelet therapy, and Grade 2 and 3 rectal toxicity occurred much more in the patients receiving the antiplatelet therapy than those without a history of antiplatelet therapy, however it was no statistically-significant difference between two groups in univariate analysis. Grade 2 and 3 rectal toxicity occurred in 3 out of 9 (33.3 %) patients with DM, while it occurred in 18 out of 177 (10.2%)patients without DM, and Grade 2 and 3 rectal toxicity occurred much more in the patients with DM than those without DM, however it was also no statistically-significant difference between two groups in univariate analysis. Regarding the correlation with dosimetric factors, there were significant differences between those with and without rectal toxicity in V70, V75, D2cc, and D1cc in HDR-BT in univariate analysis. Especially, V70 > 3.5cc, V75 > 2cc, D2cc> 7 Gy, and D1cc > 7.4 Gy were statistically-significant risk factors.
Conclusions: BED escalation could be performed without severe rectal toxicity in HDR-BT combined with EBRT. V75 >2cc, V90 > 0.2cc, D2cc > 7 Gy, D1cc > 7.4 Gy were risk factors for the incidence of rectal toxicity in HDR-BT combined with EBRT.