

(PB), to examine pre-treatment characteristics for possible selection bias and to investigate toxicity risk factors.

**Material and methods:** 322 elderly patients ( $\geq 75$ yr) with  $\geq 24$ mo follow-up were eligible for this study: 289 had EBRT (EBRT75+) and 33 had PB (PB75+). A control group of 1353 <75yr patients was used for comparison: 941 had EBRT (EBRT75-) and 412 had PB (PB75-). GU and GI toxicity (RTOG scales) were compared among the 4 groups. Pre-treatment factors: diabetes, vascular disease, PSA, Gleason score, T stage, use of hormones were analyzed. IPSS, prostate ultrasound volume were compared between PB75+ and PB75-. The above factors were examined for correlation with toxicity.

**Results:** Age group distributions for elderly patients are: 75-79yr: EBRT-255, PB-32; 80-84yr: EBRT-33, PB-1; 85-89yr: EBRT-1, PB-0. Median follow-ups are: EBRT75+: 57 mo, PB75+: 30 mo vs EBRT75-: 60 mo, PB75-: 30 mo. EBRT75+ have slightly earlier stage (T1-2: 70.2% vs 62.7%;  $p=0.008$ ) and less hormonal therapy use (37% vs 49%;  $p=0.0004$ ) comparing to EBRT75-. Pre-treatment factors are similar between PB75+ and PB75-. Toxicity between EBRT75+ and EBRT75- is similar. Toxicity between PB75+ and PB75- is similar except for late grade 3 GI toxicity: 3% (1/33) vs 0.2% (1/412) respectively;  $p=0.02$ . There is no grade 4 toxicity. PB75+ has more grade  $\geq 2$  GU toxicity (acute: 46.9% vs 29.4%;  $p=0.04$ ; late (30 mo): 42.4% vs 9%;  $p<0.0001$ ) but less grade  $\geq 2$  GI toxicity (acute: 9.4% vs 49.8%;  $p<0.0001$ ) comparing to EBRT75+. Higher pre-treatment IPSS worsened all GU toxicity outcomes (acute and late; grade  $\geq 2$  and  $\geq 3$ ;  $p<0.0002$ ) for PB group. Age group was not a significant predictor for any toxicity when other factors were controlled for.

**Conclusions:** Toxicity does not appear to be significantly affected by older age, both in EBRT and PB. Late grade 3 GI toxicity is slightly more common in PB75+, comparing to PB75-, although there was only 1 patient affected. Pre-treatment factors do not appear to be different between age  $\geq 75$  vs <75 groups and selection bias is not apparent. Older patients ( $\geq 75$ yr) have the same side effect profile as younger ones.

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POSTER

#### Prostate Cancer: up-staging effect of MRI on conformal radiotherapy planning volumes

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**Purpose:** To analyze the impact of MRI on CT defined prostate volumes for conformal radiotherapy (CFRT) due to unsuspected detection of extracapsular extension (ECE), seminal vesicle and adjacent organ involvement.

**Methods:** 104 men with localized prostate cancer who had co-registered CT and MRI simulation images between 2-2002 and 2-2005 were identified. All post-prostatectomy recurrences were excluded. A radiologist reviewed both MRI simulation images and diagnostic MRI.

Prognostic grouping was categorized into low risk (PSA <10, Gleason <7, T1, 2a stage), intermediate risk (defined as having  $\geq 1$  elevated parameter of PSA 10-20, Gleason 7, T2b, 2c) and high risk prostate cancer (defined as  $\geq 1$  elevated parameter of PSA >20, Gleason 8-10, T3, 4) with 7, 26 and 71 cases for each group respectively. The majority of the intermediate and high risk patients i.e. 89 patients received 2-3 months of hormonal therapy before simulation and MRI.

Target volumes were initially delineated on CT without prior knowledge of MRI. The treatment volumes were then edited according to the co-registered MRI. Radiotherapy volumes were corrected if there was extracapsular invasion, seminal vesicle involvement or there was invasion of other organs i.e. bladder or bowel on MRI but not suspected clinically or detected on CT.

**Results:** Mean patient age was 68 years (range 47-78). The mean initial PSA was 25.50 ng/ml (3.6-194). The median Gleason combined score was 7. The clinical prostate stage prior to MRI was of T1-2a disease in 42 patients, T2b-c in 26 and T3-4 disease in 36. MRI evidence of ECE was found in 16 cases (15%) of which unsuspected in 8 cases and required treatment volume changes to incorporate the disease. Seminal vesicle invasion was detected by the MRI in 18 patients (17%) and in 16 it was clinically not suspected. The MRI defined segment of seminal vesicle involvement was then included in the high dose radiation prostate volume. Bladder and bowel involvement, mainly focal, was found in 17 (16%) and 7 (7%) patients respectively. This bladder and bowel invasion was not evident prior to MRI in 14 and 7 of the cases respectively. The MRI involved rectal or bladder wall segment was subsequently incorporated into the prostate volume but the dose to this region was limited by dose volume constraints. Overall there were 44 instances of unsuspected MRI defined pathology that resulted in changes to the initial CT determined target volumes in 31 (29%) cases.

**Conclusions:** Diagnostic and planning MRI has resulted in substantial target volume changes for the radical irradiation of prostate cancer. MR imaging has reduced potential geographic miss and under-dosing of prostate target volume. The impact of this on clinical outcomes requires longer term follow-up.

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POSTER

#### Influence of neoadjuvant hormonal therapy on health-related quality-of-life after brachytherapy and external beam radiotherapy for localized prostate cancer

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**Background:** The aim of the study was to characterize the influence of neoadjuvant hormonal (NHT) therapy on health-related quality-of-life (HRQOL) following different radiotherapy (RT) techniques for localized prostate cancer.

**Material and methods:** A cross-sectional survey using the expanded prostate cancer index composite HRQOL instrument was administered to 196 consecutive patients following different RT modalities: external beam RT (80 patients), Ir-192 temporary brachytherapy (BT) as a boost to external beam RT (44 patients) and Ir-125 permanent BT (72 patients). To avoid bias due to a RT technique, patients with and without NHT therapy were matched according to the RT modality, so that 50% received NHT in each RT technique group. A control group consisted of 196 prostate cancer patients before the start of RT (65 with and 131 without NHT).

**Results:** Median post treatment time was 26 (range 3-50) months, median age was 72 (range 51-84) years (no statistical difference with or without NHT). NHT independently (of age, post treatment time, RT method, presence vs. absence of prognostic risk factors) diminished urinary, sexual and hormonal HRQOL compared to patients after RT only. Significantly lower scores in all domains compared to the control group without NHT were found after RT with NHT (see table). Other independent factors were Ir-192 BT for decreased urinary function, patient age for urinary incontinence scores and sexual function, and external beam RT for decreased hormonal function.

	RT with NHT (n = 98)	RT only (n = 98)	control without NHT (n = 131)
urinary function	85±20	91±15	92±14
moderate/big problem from urinary dysfunction	28%	12%	14%
bowel function	87±15	89±12	93±8
moderate/big problem from bowel dysfunction	16%	10%	5%
sexual function	19±21	31±24	39±25
hormonal function	80±25	92±16	90±15
poor or no ability to have an erection	60%	35%	24%
moderate/big problem from sexual dysfunction	50%	38%	29%

**Conclusions:** Addition of NHT to BT or external RT led to significantly diminished HRQOL. General metabolism (e.g. lack of energy) as well as the repair process during/after RT seem to be affected. NHT should be avoided for patients without the evidence for a prognostic benefit.

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POSTER

#### High dose rate brachytherapy combined with external beam radiation therapy for the treatment of prostate cancer

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**Background:** Low Dose Rate (LDR) brachytherapy combined with external beam radiation therapy (EBRT) has been used for quite some time for the treatment of cancer of the prostate. However, LDR brachytherapy is associated with considerable genitourinary side effects. We have incorporated HDR brachytherapy using Ir-192 into the treatment regimen to avoid these side effects.

**Methods:** Since January 2001, 185 patients with early prostate cancer stage T1, 2NO were treated with a protocol of combined external beam radiation and HDR brachytherapy. External beam radiation was delivered using 3D conformal radiation therapy or Intensity Modulated Radiation

Therapy (IMRT) with a tumor dose of 45–50.4 Gy to the prostate. HDR prostate brachytherapy was performed as an outpatient procedure after a period of four weeks under spinal anesthesia with two fractions two weeks apart. A dose of 10 Gy was delivered to the prostate capsule within a 0–2 mm margin with a 12 Gy delivered to the peripheral zones. The dose to the rectum and urethra was limited as not to exceed 10 and 12 Gy respectively. Dose optimization was achieved using CT image based ABACUS algorithm.

**Results:** The results showed a substantial decrease in early genitourinary side effects when compared to another group of 326 patients previously treated at this facility with LDR brachytherapy. HDR brachytherapy enabled to deliver conformal dose distribution to the prostate and avoided areas of hot spots close to the bladder and rectum. Patients with large volume prostates could also be adequately treated which was not feasible with LDR brachytherapy. The data for 130 patients (out of 185) treated with HDR brachytherapy and external beam combination was reviewed. On the Urinary Symptom Score (Scale 1–35), 73% of patients reported normalcy, 20% mild, 6.2% moderate, and 0.8% reported severe toxicity. Two patients (1.5%) had reported episodes of rectal bleeding. One patient reported frequent fecal urgency. Preliminary results show excellent biochemical control.

**Conclusions:** Our experience shows that treatment of prostate cancer using external beam radiation and HDR brachytherapy results in minimal genitourinary side effects and better patient tolerance. Long term follow-up is being conducted to evaluate the outcome of this combination therapy.

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POSTER

#### Cone beam CT for daily image-guidance in prostate radiotherapy

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**Purpose:** The use of highly conformal radiotherapy fields for the treatment of prostate cancer has permitted radiation dose escalation, with improved biochemical relapse-free survival demonstrated. One of the major limitations of conformal radiotherapy techniques (CRT) is the smaller margin of error for treatment set-up and delivery. Daily visualization of prostate position before treatment allows correction of set-up errors and reduction of radiation field margins. At Princess Margaret Hospital megavoltage electronic portal imaging (EPI) of fiducial markers implanted into the prostate is performed as a surrogate of prostate position for daily localization. Kilovoltage cone-beam CT (CBCT) is new technology that acquires 3-dimensional volumetric datasets of the patient at the time of treatment and permits visualization of soft tissue organs. This study compares the two image guidance methods.

**Methods:** Fifteen patients with prostate cancer received CRT (79.8 Gy in 42 fractions) with daily on-line image guidance using EPI for localization of 3 fiducial markers implanted in the prostate. CBCT images were acquired prior to set-up correction. The CBCT images were retrospectively analyzed for geometric displacement of the prostate gland. Auto segmentation was used for fiducial marker matching and a manual contour alignment tool was used for soft tissue matching (prostate contour) with markers digitally removed. The CBCT predicted shifts based on the soft-tissue and fiducial marker match were compared to the applied shifts of the EPI.

**Results:** There was high correlation between CBCT and EPI fiducial marker matching in all directions, with  $R^2$  values of 0.95 right-left, 0.84 anterior-posterior, and 0.82 superior-inferior. Correlations for soft-tissue matching were 0.92 right-left, 0.49 anterior-posterior and 0.55 superior-inferior.

**Conclusion:** CBCT provides accurate 3D localization of prostatic fiducial markers. Greater discrepancies between EPI and soft-tissue matching were observed. This can be attributed to the inherent differences in the characteristics of each guidance system and the difficulties in accounting for rotations and deformations. This study shows that soft-tissue matching of the prostate is feasible with CBCT. CBCT also provides additional information on prostate deformation and volume changes during treatment and this is currently being evaluated.

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POSTER

#### Optimized image-guided radiation therapy protocol for the prostate

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**Background:** Radiation therapy typically relies on a single pre-treatment CT to measure patient anatomy. It is apparent that patients are dynamic

systems, however, and can change between fractions and even during a single fraction. In contrast, modern image-guided radiation therapy (IGRT) procedures provide multiple views inside the patient and allow one to consider the statistics of organ motion. The goal of this study was to view the treatment of prostate cancer from such a 4D perspective and to design an appropriate IGRT treatment protocol balancing the need for efficiency and accuracy.

**Methods:** Ten patients were treated for prostate cancer using CT-based IGRT. The CT-on-rails system allows patients to be scanned on the treatment table immediately before radiation is applied. After scanning, a daily adjustment is calculated to correct for any setup variation or organ motion. The patient is then shifted using the treatment table to offset the calculated adjustment and radiation therapy proceeds as usual. Cumulative data from each of the ten patients was retrospectively analyzed to determine the statistical nature of the IGRT shifts.

**Results:** An average shift was calculated for each patient over all the shifts recorded during the first treatment phase (typically 25 fractions). This average was then compared to a partial average calculated from a smaller number of sequential shifts. It was shown that averaging the first five shifts predicted the true average to within 3 mm's for most cases, and averaging the first 10 shifts reliably yielded accuracy better than 2 mm's.

**Conclusions:** Based on these results, we recommend the following protocol. IGRT prostate patients should be scanned before and after treatment for the first five fractions. The average shift calculated from these 10 sample points can then be used to predict the average prostate position for the remaining fractions (if convergence appears likely). Scanning before and after reduces the time required to collect 10 sample points and measures any systematic intra-fraction changes such as those previously reported by us. A single CT scan once weekly can then be used for the remaining fractions to replace port films for setup verification. The total dose from daily CT scans at our clinic has been estimated to be lower than weekly orthogonal port films, and this protocol would further reduce that dose while maintaining reasonable treatment accuracy.

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POSTER

#### 10 Years follow-up of 665 patients with prostate adenocarcinoma treated with 3 dimensional-CT guided brachytherapy with a pararectal approach

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**Background:** Prostate brachytherapy is a common treatment option for prostate cancer. Transrectal ultrasound-guided transperineal brachytherapy as a monotherapy is not recommended in patients with large volume prostate glands (>60 cm<sup>3</sup>), pubic arch interference, medial lobe hypertrophy protruding in the urinary bladder, prostate calculi, post-transurethral prostate resection (TURP), obesity, penile prosthesis and patients without a rectum due to previously excised colorectal cancer. Aim of the study is to report 10 year treatment results of prostate cancer patients (including the above mentioned subgroups), who underwent brachytherapy using a three-dimensional computer-tomography guided stereotactic system via a pararectal approach.

**Material and Methods:** 665 patients were treated with brachytherapy for prostate cancer (June 1994 to May 2002). A 3D-stereotactic system, posterior pararectal approach and CT guidance was used for brachytherapy in these patients. The prescribed radiation dose was 120–144 Gy with Iodine 125 seeds in rapid-strand format. The patients' age range was 42–90 years (Mean 67.2, Median 68). Patients were divided into 3 risk profile groups (Low Risk: PSA <10, Gleason <7, Stage ≤T2a No Mo, n = 172 Patients; Intermediate Risk: PSA 10–20 only or Gleason = 7 only, Stage ≤T2a No Mo, n = 87 Patients; High Risk: Gleason >7, PSA >20, Stage ≥T2b, or 2 intermediate Risk Factors, n = 406 Patients). 59 patients had biopsy proven seminal vesical invasion. Prostate Volume Range was 14–180 cm<sup>3</sup> (41% had prostate glands greater than 60 cm<sup>3</sup>). Patient follow-up included clinical examination and serum PSA every 3 months the first 2 years, every 6 months up to 5 years and yearly after the 5<sup>th</sup> year. Median follow-up was 4 years.

**Results:** Biochemical no evidence of disease was 95% for low risk patients, 94% for intermediate risk and 89% for high risk patients. Disease free survival (DFS) was considered for patients who had no 3 consecutive PSA rises requiring androgen ablation. Median nadir was lower than 0.1 ng/ml. There was a significant difference between patient with low or intermediate risks and patients with high risk, whereas there was no significance in the DFS between the low and intermediate risk patient group (High to intermediate risk p = 0.005, High to low risk p = 0.001, low to intermediate