Effect of dose and image guided radiotherapy (IGRT) on erectile potency (EP) in prostate radiotherapy

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Purpose or Objective:
IGRT enables accurate target volume localisation, potentially permitting reduced treatment margins, which may decrease normal tissue toxicity. Erectile dysfunction is a common toxicity of prostate RT and the penile bulb (PB) is suggested as a surrogate for undetermined structures critical for erectile function. However, PB dose-volume effects are not well established. We aim to determine dose-response characteristics of the PB in prostate cancer patients treated using IGRT with standard and reduced margins.

Material and Methods:
Men with previously untreated localised prostate cancer were randomised within the multicentre CHHiP (Conventional or Hypofractionated High dose Intensity Modulated Radiotherapy for Prostate Cancer) IGRT sub-study (CRUK/06/16). Men were randomised to receive 2Gy or 3Gy per fraction, delivered either with or without daily online image-guidance, with standard or reduced CTV-PTV margins. Short course hormone therapy (HT) was allowed and details were recorded. EP was assessed at baseline, pre-RT and at 6 monthly intervals to 2 years, then annually to 5 years post-RT. EP was physician graded as normal erection (G0), decreased (G1), absent (G2) and unknown. Analysis included the subset of men treated with IGRT within the sub-study with an EP assessment at 2 years.

Planning CT scans and reference dose distributions were imported into analysis software (Vodca, MSS GmbH). The PB was retrospectively contoured using established anatomical boundaries (1) and published guidelines (2,3) by one clinician. In-house software was used to convert the hypofractionated plan into equivalent dose in 2Gy per fraction using the Withers formula ($\alpha/\beta = 3$Gy). PB dose-volume (DVH) parameters were evaluated against EP at 2 years using atlases of complication incidence (ACI) (Matlab, Mathworks, Natick, MA) for G2 EP. Dose-volume constraints were derived using ROC analysis (Youden index) and assessed against the no information rate.

Results:
Between June 2010 and June 2011, 293 men entered the study. Complete dose-EP data sets were available for 129 men treated with IGRT. 14/129 men had G2 EP at baseline and were excluded. At 2 years, 27/52 (52%) men treated with standard margins (IGRTS) and 25/63 (40%) men treated with reduced margins (IGRTR) had G2 EP. HT characteristics between the two groups were similar. The PB volume was 7.1(±2.8)cm³ in IGRTS group and 6.5(±2.5)cm³ in IGRTR group. The reduced margins resulted in a reduction in dose to the PB and statistically significant dose-volume constraints for G2 EP were derived for 45, 50, 55, 60 and 65Gy (Table 1). The ACI is presented in Figure 1 and demonstrates a dose-volume response.

<table>
<thead>
<tr>
<th>G1 symptom</th>
<th>Peak Incidence W4 - W6 (%)</th>
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<tbody>
<tr>
<td></td>
<td>HF</td>
<td>SF</td>
<td>p</td>
<td>3DCRT</td>
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<tr>
<td>Blood loss</td>
<td>15.1</td>
<td>7.6</td>
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<td>Mucus loss</td>
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<td>39.4</td>
<td>0.110</td>
<td>51.9</td>
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<tr>
<td>Loose stools</td>
<td>52.5</td>
<td>42.8</td>
<td>0.025</td>
<td>56.1</td>
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<td>Stools 4+</td>
<td>34.7</td>
<td>25.8</td>
<td>0.018</td>
<td>42.9</td>
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<tr>
<td>Incontinence</td>
<td>19.5</td>
<td>14.0</td>
<td>0.100</td>
<td>21.8</td>
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<tr>
<td>Diarrhea</td>
<td>16.5</td>
<td>13.4</td>
<td>0.290</td>
<td>12.6</td>
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</table>
Conclusion: There is evidence to suggest a dose volume effect between the PB and EP. Discriminatory PB dose-volume constraints were found to predict G2 EP. Further analysis is in progress to include patient reported outcomes related to EP.

Ref: (1) Wallner, IJROBP 2002 (2) Perna, Rad Onc 2011 (3) Gay, IJROBP 2012

OC-0341

Anal dose reduction for radiotherapy of prostate cancer does not lead to less rectal incontinence

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Purpose or Objective: Radiation-induced rectal incontinence has a negative impact on Quality of Life in patients irradiated for prostate cancer. Several studies identified dose-effect relationships for the anal canal and lower rectum and hence, dose constraints for treatment planning have been implemented. We studied patients reported rectal incontinence in a population treated with Image-guided intensity modulated radiotherapy (IG-IMRT) and planned with a dose constraint for the anal canal, and compared it with a reference population treated with 3D-conformal radiotherapy (3D-CRT) with no dose constraint for the anal canal. For that purpose we analyzed data from two large prospective cohorts.

Material and Methods: We selected patients treated to 78Gy (39x2Gy) from two trials (CKTO 96-10 and CKTO 2006-08), who completed at least 2 follow-up questionnaires which included questions on pad use and fecal incontinence (IGIMRT group n=242, 3DRT group n=189). In the IG-IMRT group, mean dose to the anal canal was restricted to 58 Gy per protocol (more strict constraints depended on local planning guidelines). Grade ≥2 (G≥2) incontinence was defined as use of pads for uncontrollable loss of feces or mucus, Grade (G≥1) incontinence was defined as any reported fecal incontinence regardless use of pads. Prevalence and cumulative incidences of G≥2 and G≥1 incontinence were calculated. Cox regression was used to calculate Relative Risks (RR).

Results: Planned mean dose to the anal canal was on average 44.6 Gy (range 17-65) for 3D-CRT and 23.6 Gy (range 3-50) for IG-IMRT (p=0.001). Median follow-up was 60 months. The 5y cumulative incidence of G≥2 incontinence was 15.2% for IG-IMRT vs 14.9% for 3D-CRT (RR=1.02, p=0.9). Prevalence of G≥1 incontinence was 5% at baseline and in the range of 30% - 40% in the years after treatment, with no significant differences between the groups (Figure 1). Within the 3D-CRT group, previous abdominal surgery was predictive for G≥2 incontinence (RR=2.9, p=0.05), whereas age >70 years at start RT (RR=2.9, p=0.01), diabetes mellitus (RR=2.4, p=0.04), and seminal vesicle dose 70 Gy vs 0 Gy (RR=9.2, p=0.03) were predictive in the IG-IMRT group. At multivariate analysis, adjusting for the significant baseline factors, RR of mean anal canal dose was 1.00 (p=0.9) for IG-IMRT patients and 1.05 (for each increase of 1 Gy) for 3D-CRT (p=0.04). Acute toxicity G2 (mainly proctitis) was predictive (p<0.01) in both groups with a RR of 3.1 (IG-IMRT) and 4.1 (3D-CRT). G≥1 incontinence at any time during follow-up was significantly associated with abdominal surgery in the 3D-CRT group, and with age >70 years, and diabetes mellitus in the IG-IMRT group.

Conclusion: IG-IMRT with anal canal dose constraints did not reduce long-term incidence of rectal incontinence in prostate cancer patients, despite significantly reduced dose levels to the anal canal region. Further investigations are needed to understand the mechanisms of radiation damage causing rectal incontinence.

OC-0342

Chemoradiotherapy in high-risk prostate cancer (QRT SOGUG trial): Preliminary report

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Purpose or Objective: To assess the toxicity and feasibility of concomitant radiotherapy with low doses of docetaxel plus standard hormonal treatment in patients with high risk localized prostate cancer.

Material and Methods: Patients were randomly assigned to either arm A (LH-RH analogs every 3 months for 3 years and radiotherapy 74 Gy [20Gy x 37 fractions]) or arm B (LH-RH analogs every 3 months for 3 years, radiotherapy 73.8 Gy [1.8 Gy x 41 fractions]) and concurrent weekly docetaxel at 20 mg/m2 for 9 weeks). Chemotherapy was started one week before of radiotherapy. Primary endpoint was PSA relapse according to the Phoenix definition. The planned number of patients was 130 to detect a 15% difference with a power of 80% and an alpha of 0.05 (two-sided).

Results: From 12/2008 to 9/2012, 130 pts were accrued (Arm A: 64, Arm B: 66). Median age was 68 years (61-73). Patients had T3-T4 (82.6%), Gleason Score 8 (76.3%), PSA > 20 ng/mL (26.9%) and pN+ (18.9%). All characteristics were well-balanced between arms. Median dose of radiotherapy was 74 Gy (72-74.8) in arm A, and 73.8 Gy (72-75.6) in arm B. 75.7% of patients received the planned 9 treatments of docetaxel and median number of cycles delivered per patient was 9. After a median follow-up of 29.6 months (9.6-40.2), most common grade 1/2 toxicities (arm A and arm B) were: cystitis (12.5% vs 8.3%), diarrhea (35.9% vs 70%), proctitis (12.5% vs 13.3%), rectal tenesmus (3.1% vs 23.3%), asthenia (23.4% vs 61.6%) and dysuria (28.1% vs 30.0%). Toxicity grade≥3, diarrhea was reported in 8.3% of patients in arm B and 0% in arm A. Grade≥3 lymphopenia occurred less often in arm A than in arm B (3.1% vs 23.3%). There was no toxicity-related death.

Conclusion: The QRT SOGUG phase IIb trial shows that standard doses of radiotherapy and concurrent weekly docetaxel can be administered without increasing toxicity profile.