Radiation-induced late rectal toxicity for IMPT vs VMAT in patients with localized prostate cancer

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Purpose or Objective
An ongoing multicenter observational study, registered at ClinicalTrials.gov, is assessing the intestinal, hematologic and urinary toxicity from whole-pelvis radiotherapy (WPRT) in the radical, adjuvant or salvage RT treatment of prostate cancer. The Inflammatory Bowel Disease Questionnaire (IBDQ) is used to evaluate radiation-induced Intestinal Toxicity (IT): it explores 10 Bowel symptoms and their possible detrimental effect on Emotional, Social and Systemic Domains. The responses are scored from 7 (best function) to 1 (worst). This analysis focuses on acute IT.

Material and Methods
Patients (pts) treated with conventional fractionation or moderate hyperfractionation are included. Static-field IMRT (SS-IMRT), Tomotherapy (TOMO) and VMAT are allowed. WPRT is at the discretion of the referring radiation oncologist. The IBDQ was completed at baseline, at RT mid-point and end. For this analysis, focused on the first 303 pts with complete IBDQ at baseline and radiotherapy mid-point and end, a worsening in single bowel symptoms ≥3 points was set as endpoint for IT definition. This worsening corresponds to 50% of the total possible score, which could be of interest from a clinical perspective. The largest IBDQ worsening between baseline and RT mid-point or end was considered. Associations between IT and patient/treatment related factors were evaluated through logistic regression (LR). Further analyses were performed to identify the symptoms more closely associated with detriment in Social, Emotional and Systemic domains.

Results
303 pts having the complete set of IBDQs were considered. Eight per cent were treated by means of SS-IMRT in sparing bowel volumes receiving 40-50 Gy. Rates of significant worsening for each symptom are reported in Table 1a. SS-IMRT was associated with an increased risk (OR ≈0.3, p=0.01÷0.05) of abdominal pain, cramps, rectal bleeding and nausea as a possible consequence of the reduced ability impacts abdominal pain, cramps, rectal bleeding and nausea, as a possible consequence of the reduced ability of SS-IMRT in sparing bowel volumes receiving 40-50 Gy. Social domain is highly influenced by frequent bowel movements and loose stool, while rectal bleeding impacts Emotional wellbeing.

Conclusion
Even in the era of modern IMRT, WPRT-induced IT is non-negligible, leading to moderate/severe symptom rates ranging from 7 to 50%. Extended WPRT fields are related to increased abdominal pain/cramps, while RT technique impacts abdominal pain, cramps, rectal bleeding and nausea, as a possible consequence of the reduced ability of SS-IMRT in sparing bowel volumes receiving 40-50 Gy. Social domain is highly influenced by frequent bowel movements and loose stool, while rectal bleeding impacts Emotional wellbeing.

PO-0821 Radiation-induced late rectal toxicity for IMPT vs VMAT in patients with localized prostate cancer
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Purpose or Objective
Over the years, multiple NTCP models have been published regarding radiation-induced late rectal toxicity, but only a few included other toxicities besides rectal bleeding. Peeters et al.1 published NTCP models for high stool frequency, fecal incontinence and rectal bleeding.

Recent improved planning techniques for photon therapy (VMAT dual-arc) as well as proton therapy (CTV-based robust IMPT) could further reduce late rectal toxicity. The purpose of this in silico planning study was to assess predicted radiation-induced late rectal toxicity after treatment of localized prostate cancer for these modern photon and proton techniques.

Material and Methods
For this study, 20 planning-CT scans were used of patients treated at our department in 2015-2017 for localized prostate cancer. The dose prescription included 77 Gy(RBE) to the prostate (and part of/whole vesicles), and 70 Gy(RBE) to (part of) the vesicles (depending on tumor stage), where RBE=1.1. The CTV-PTV margin for the photon plans was 5 mm laterally and 6 mm in other directions. Proton therapy plans were robustly optimized using 5 mm setup laterally and 6 mm in other directions and 3% range uncertainty. Plans were evaluated for robustness using shifts in 26 directions (photons and protons) and range uncertainties +/-3% (only protons). Plans were optimized until ≥98% of the CTV was covered with ≥95% of the dose in the voxel wise minimum scenario. Late rectal toxicity grade ≥2 was assessed using NTCP models of Peeters et al.1 for rectal bleeding, stool frequency and fecal incontinence.

Results
Overall, most proton plans resulted in a slightly lower predicted incidence of late rectal toxicity than the photon plans (Figure 1). Most absolute differences were seen for

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Table 1a: Symptom worsening from baseline to RT mid-point and end for IMRT, TOMO and VMAT.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>IMRT</th>
<th>TOMO</th>
<th>VMAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>0.2</td>
<td>0.2</td>
<td>0.4</td>
</tr>
<tr>
<td>Rectal bleeding</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
</tr>
<tr>
<td>Frequency</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Incontinence</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
</tr>
</tbody>
</table>

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Table 1b: Predicted incidence of late rectal toxicity for IMRT, TOMO and VMAT.

<table>
<thead>
<tr>
<th>Technique</th>
<th>Predicted Incidence (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMRT</td>
<td>20</td>
<td>0.05</td>
</tr>
<tr>
<td>TOMO</td>
<td>15</td>
<td>0.05</td>
</tr>
<tr>
<td>VMAT</td>
<td>10</td>
<td>0.05</td>
</tr>
</tbody>
</table>
Patient-reported outcomes after A. Lazo cancer. hypofractionated radiotherapy to 66Gy for prostate proton therapy.

0-5% of the patients with localized prostate cancer for the use of above mentioned NTCP models and endpoints relative to VMAT. Application of the Dutch guideline and for late rectal toxicity and thus have a potential benefit CTV-based robust IMPT resulted in slightly lower NTCP’s

Conclusion

frequency after conformal radiotherapy for prostate

Rectal bleeding, fecal incontinence and high stool frequency after conformal radiotherapy for prostate cancer treatment with proton therapy, which was a patient with endpoint fecal incontinence (with history of abdominal surgery).

Figure 1: Late rectal toxicity

Conclusion
CTV-based robust IMPT resulted in slightly lower NTCP’s for late rectal toxicity and thus have a potential benefit relative to VMAT. Application of the Dutch guideline and the use of above mentioned NTCP models and endpoints would lead to a relative small selection of approximately 0-5% of the patients with localized prostate cancer for proton therapy.

References

PO-0823 Patient-reported outcomes after hypofractionated radiotherapy to 66Gy for prostate cancer.

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Purpose or Objective
Purpose: to evaluate biochemical control, toxicity and patient function after prostate cancer treatment with moderate hypofractionated and dose-escalated image-guided volumetric modulated arc therapy (VMAT) for localized prostate cancer in an observational study.

Material and Methods
Material and methods: From 2010 to 2017, men with localized prostate cancer (from low to high-risk) who received VMAT to a dose of 66 Gy in 22 fractions of 3 Gy, and had over 2 years follow-up, were eligible. After the treatment, patients were followed every three months the first two years and then every six months. Endpoints included acute toxicity at the end of treatment and late gastrointestinal (GI) and genitourinary (GU) toxicity using the Radiation Therapy Oncology Group (RTOG) scoring, biochemical control and patient reported outcomes using the Expanded Prostate Cancer Index (EPIC-26).

Results
Results: One hundred and sixteen men became eligible. With a median follow-up of 40 months, acute GI and GU Grade2 toxicity were 26% and 12%, respectively. Cumulative late Grade2 GI and GU toxicity was 1% and 4% respectively. No Grade3 acute or late toxicity were reported. Biochemical control was 97%. Ninety patients (78%) completed the EPIC-26 form. Patient-reported outcomes showed no urinary and bowel general problems in 76% and 91%, respectively. The proportion of patients reporting moderate urinary problems was 2,2% (2 patients). No moderate or severe bowel problems were reported.

Conclusion
Conclusion: Dose escalation to 66 Gy with moderate hypofractionated VMAT is associated with favourable late toxicity, biochemical control and good patient reported outcomes with over two years follow-up.

PO-0823 TRAC: Automated atlas based machine learning QA of contouring accuracy for the PROMETHEUS trial

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Purpose or Objective
Variation in radiotherapy target volume and OAR delineation is one of the largest contributing factors to the global uncertainty in treatment delivery. Further, it is acknowledged that it is also an obstacle to effective clinical trials in advanced treatment techniques if not accounted for in the experimental design. However, manual expert review of delineation for all patients enrolled prior to treatment is logistically arduous and expensive. We propose a scalable cloud based automated solution for trial specific review of delineation accuracy, The Radiotherapy Atlas Contouring (TRAC) tool. TRAC has the added benefit of enabling rapid clinical translation of study findings into regular practice.

Material and Methods
Retrospective data from the prostate SBRT trial PROMETHEUS (ACTRN12615000223538) was utilised for this study. Multi-atlas generation consisted of MRI data from 10 patients, five observers, three anatomical structures and a rectal stabilisation device. The rectal stabilisation devices approved for use in the study included the RectaFix® and SpaceOAR® hydrogel. Tolerance for delineation acceptability was based on observer variation in multi-atlas generation. Where necessary the manual expert reviewer delineated a corrected contour for comparison. Thus, for each patient there were a number of structures deemed correct and incorrect by manual review for testing. A random forest classifier was trained using a number of contour features (DSC, Components, Volume, Elongation, Perimeter,