Results
Mean anorectal dose and surface > 70 Gy (570) were 29.0 Gy vs 29.5 Gy (p=0.4) and 14.2% vs 12.6% (p=0.01), for HF and SF, respectively. Differences between hospitals varied between 24.7 Gy-33.2 Gy (average mean dose) and 10.4%-16.1% (average 570), and were significant (p<0.01).

Patient-reported GI symptoms of blood loss (p=0.001) and use of pads (p=0.01) were significantly higher in the HF group (FIG 1); pain with stools, abdominal cramps, and diarrhea were not increased and mucus loss was non-significantly increased (p=0.07). Significant differences between hospitals were observed for all complaints, except rectal pain (FIG 2). In general, the hospital with rectal balloon (D) and hospital with MRI delineation (A) showed favorable dose parameters and symptom patterns compared to the other hospitals. Patients treated with a rectal balloon reported relatively low symptom rates but at the same time, prescribed medication for GI complaints was reported more frequently as well (14% doctor’s reported versus 4% for the other hospitals).

Conclusion
We conclude that the HF schedule was associated with slightly larger rectal high-dose volumes assuming an α/β of 3 Gy, and a significantly higher risk of rectal bleeding and use of pads. Furthermore, we found that variation in local treatment protocols had a significant impact on rectal dose and toxicity risks, despite the use of similar techniques and identical dose prescriptions.

Fig 1: Probability of nodal involvement (p), x1=cT-stage (see Tab.1), x2=percentage of positive cores

\[ P = \frac{1}{1 + e^{-(-7.973 + 1.022x_1 + 0.021x_2)}} \]

Tab. 1: Definition of variable x1
cT-stage Variable x1
cT1c 1
cT2a 2
cT2b 3
cT2c 4
cT3a 5
cT3b 6
cT4a 7

Conclusion
We developed a new formula based on SN-dissection excluding only two parameters in contrast to other nomograms. The new formula is based on SN dissection which is comparable to extended node dissection. The prediction accuracy of the new formula was comparable to the best nomogram i.e. the Briganti nomogram. In general, accuracy of nomograms including the new formula was improved when T-stage was based on MRI.

OC-0128 Patient-reported outcome in the prostate HYPRO trial: gastrointestinal toxicity
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Purpose or Objective
The phase 3 HYPRO trial, randomizing to 19x3.4 Gy hypofractionation (HF) or 39x2 Gy standard fractionation (SF), recently reported that the hypothesized non-inferiority of the HF schedule was not proven for late Grade ≥2 gastrointestinal (GI) toxicity, neither was there a significant difference observed for GI Grade ≥2 and Grade ≥3 with 5y follow-up. The aim of this analysis was to compare dose parameters and patient-reported late GI symptoms between SF and HF, and between hospitals of treatment.

Material and Methods
Patients with localized prostate cancer from four hospitals applying Image-Guided IMRT protocols and recruiting >70 patients were analyzed. Patients (n=578; 284 SF, 294 HF) with ≥1 follow-up symptom questionnaire were eligible (n=2442). Protocol dose constraints were: mean dose anal canal <58 Gy and rectal volume <50% receiving ≥65 Gy, using a 0 mm margin towards rectum for the boost. Local guidelines were applied for delineation, dose (inhomogeneity, margins (5-8 mm), and further optimization. One hospital applied a rectal balloon and another hospital delineated the prostate on MRI. Incidences of GI symptoms for the period 0.5y-5y post-RT were compared between treatment arms and hospitals. Medication prescription was evaluated as well. Anorectal dose parameters (EQD2) were calculated with α/β=3 Gy. The effect of hospital and treatment on the incidence of complaints was estimated in a multivariate model including follow-up time. Treatment groups were well balanced within hospitals and over time.
Results

Median follow-up was 61 months. Two LR patients (1.7%) and two IR patients (1.5%) experienced grade 3 toxicities, far below the 10% toxicity rate deemed excessive (P=0.001 for both cohorts). There were no grade 4-5 toxicities. All grade 3 toxicities were GU and occurred between 11 and 51 months after treatment. For the entire group, actuarial 5-year overall survival was 95.6%, and DFS was 97.1%. In LR patients, the 5-year DFS was 97.3%, which was superior to 93% DFS from historic controls (p=0.014). 5-year DFS was 97.1% for IR patients.

Patient-reported QOL outcomes are described in the table below. Clinically relevant declines in urinary irritative scores from were observed at 1 and 12 months after treatment, with subsequent return to baseline. A fall in bowel QOL was seen at 1 month only. The gradual decline in sexual QOL did not reach clinical relevance.

<table>
<thead>
<tr>
<th>Follow-up interval:</th>
<th>Baseline</th>
<th>1 mo</th>
<th>6 mo</th>
<th>1 yr</th>
<th>2 yr</th>
<th>3 yr</th>
<th>4 yr</th>
<th>5 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td># responses:</td>
<td>298</td>
<td>294</td>
<td>210</td>
<td>263</td>
<td>265</td>
<td>223</td>
<td>191</td>
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<tr>
<td>Incontinence:</td>
<td>93.5</td>
<td>90.3</td>
<td>90.8</td>
<td>87.7</td>
<td>88.9</td>
<td>89.2</td>
<td>87.6</td>
<td>88.5</td>
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<tr>
<td>Irritative:</td>
<td>87.6</td>
<td>75.0*</td>
<td>84.8</td>
<td>80.0*</td>
<td>87.2</td>
<td>89.7</td>
<td>89.0</td>
<td>90.3</td>
</tr>
<tr>
<td>Bowel:</td>
<td>94.8</td>
<td>83.4*</td>
<td>92.1</td>
<td>90.8</td>
<td>92.2</td>
<td>93.0</td>
<td>92.3</td>
<td>92.5</td>
</tr>
<tr>
<td>Sexual:</td>
<td>56.2</td>
<td>53.7</td>
<td>51.1</td>
<td>43.8</td>
<td>47.8</td>
<td>47.6</td>
<td>45.8</td>
<td>43.1</td>
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*—clinically relevant

Conclusion

Dose-escalated prostate SBRT can be safely administered across multiple institutions. In LR patients, 5-year DFS rates are superior to historical EBRT control rates. In IR patients, 5-year DFS also appears favorable. Declines in GI and GU QOL are transient. SBRT is a suitable option for low- and intermediate-risk prostate cancer.

Purpose or Objective

Single-institution studies suggest SBRT is a cost-effective alternative to external-beam RT for prostate cancer. We hypothesized that dose-escalated SBRT could be safely administered across multiple institutions, and that in low-risk (LR) patients, dose escalation would improve 5-year disease-free survival (DFS) rates compared to historic controls. We now also report 5-year quality of life (QOL) outcomes.

Material and Methods

21 centers enrolled 309 evaluable patients with biopsy-proven prostate adenocarcinoma: 172 with low-risk, and 137 with intermediate-risk (IR) disease. All patients were treated with a non-coplanar robotic SBRT platform using real-time tracking of implanted fiducials. The prostate was prescribed 40 Gy in 5 fractions of 8 Gy. Toxicities were assessed using CTCAE v3 criteria, and biochemical failure using the nadir+2 definition. Study populations yielded 90% power of identifying excessive (>10%) rates of grade 3+ GU or GI toxicities, and in the LR group, 80% power of showing improvement in DFS over a historic comparison control rate of 93%.

QOL for urinary, bowel and sexual function were assessed using the Expanded Prostate Cancer Index Composite (EPIC-26) questionnaire. Outcomes were analyzed with a longitudinal analytic approach using generalized estimating equations; the dependent variable was change in scores from baseline. Post-SBRT domain score differences were considered clinically relevant if they exceeded 1/2 standard deviation of pre-treatment scores.

Patient-reported QOL outcomes are described in the table below. Clinically relevant declines in urinary irritative scores were observed at 1 and 12 months after treatment, with subsequent return to baseline. A fall in bowel QOL was seen at 1 month only. The gradual decline in sexual QOL did not reach clinical relevance.

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