

TABLE S1. Matching variables for all patients and those selected for the matched-pair analysis.

| Matching variable | All patients (Pre-Matching) | | | Matched patients (Post-Matching) | | |
|------------------------------------|-----------------------------|-------------------------|---------|----------------------------------|-------------------------|---------|
| | IMRT (57 Pat) | | p-value | IMRT (29 Pat) | | p-value |
| | Pat (%) | PBT (31 Pat) Pat (%) | | Pat (%) | PBT (29 Pat) Pat (%) | |
| Diabetes mellitus | | | 0.073* | | | 0.76* |
| Yes | 9 (15.8) | 10 (32.2) | | 7 (24.1) | 8 (27.6) | |
| No | 48 (84.2) | 21 (67.7) | | 22 (57.9) | 21 (72.4) | |
| TUR-P | | | 0.92* | | | 0.55* |
| Yes | 4 (7.0) | 2 (6.5) | | 1 (3.4) | 2 (6.9) | |
| No | 53 (93.0) | 29 (93.5) | | 28 (96.6) | 27 (93.1) | |
| Risk group D'Amico | | | 0.85† | | | 0.35† |
| Low | 5 (8.8) | 2 (6.5) | | 0 (0.0) | 2 (6.9) | |
| Intermediate | 41 (71.9) | 24 (77.4) | | 23 (79.3) | 22 (75.9) | |
| High | 11 (19.3) | 5 (16.1) | | 6 (20.7) | 5 (17.2) | |
| Anticoagulants | | | 0.22* | | | 0.58* |
| Yes | 26 (45.6) | 10 (32.3) | | 11 (37.9) | 9 (31.0) | |
| No | 31 (54.4) | 21 (67.7) | | 18 (62.1) | 20 (69.0) | |
| Prostate volume in cm ³ | | | 0.007‡ | | | 0.35‡ |
| median (range) | 61 (23 - 119) | 51 (22 - 99) | | 53 (32 - 119) | 51 (22 - 99) | |

Abbreviations: Pat, patients; TUR-P, transurethral resection of the prostate; IMRT, intensity-modulated radiotherapy; PBT, proton beam therapy.

* Exact Fisher test

† χ^2 test

‡ Mann-Whitney U test

TABLE S2. Questionnaire response rates for complete pairs at different time points.

| Item | Baseline | 3 m after RT | 12 m after RT |
|-----------------------------------|-----------|--------------|---------------|
| | No (%) | No (%) | No (%) |
| EORTC QLQ-C30 | | | |
| Functional scales | | | |
| Global health status | 21 (72.4) | 18 (62.1) | 11 (37.9) |
| Role functioning | 22 (75.9) | 17 (58.6) | 10 (34.5) |
| Emotional functioning | 22 (75.9) | 18 (62.1) | 11 (37.9) |
| Physical functioning | 23 (79.3) | 19 (65.5) | 11 (37.9) |
| Social functioning | 22 (75.9) | 17 (58.6) | 10 (34.5) |
| Cognitive functioning | 22 (75.9) | 18 (62.1) | 10 (34.5) |
| Symptom scales | | | |
| Pain | 18 (62.1) | 17 (58.6) | 11 (37.9) |
| Diarrhoea | 22 (75.9) | 18 (62.1) | 10 (34.5) |
| Fatigue | 22 (75.9) | 19 (65.5) | 11 (37.9) |
| Insomnia | 22 (75.9) | 19 (65.5) | 11 (37.9) |
| Constipation | 22 (75.9) | 18 (62.1) | 10 (34.5) |
| Nausea and vomiting | 22 (75.9) | 19 (65.5) | 11 (37.9) |
| Appetite loss | 21 (72.4) | 19 (65.5) | 11 (37.9) |
| Dyspnoea | 22 (75.9) | 19 (65.5) | 11 (37.9) |
| Financial difficulties | 22 (75.9) | 18 (62.1) | 11 (37.9) |
| EORTC QLQ-PR25 | | | |
| Symptom scales | | | |
| Urinary symptoms | 22 (75.9) | 18 (62.1) | 11 (37.9) |
| Incontinence aid | 11 (37.9) | 16 (55.2) | 11 (37.9) |
| Bowel symptoms | 12 (41.4) | 17 (58.6) | 10 (34.5) |
| Hormon treatment related symptoms | 11 (37.9) | 17 (58.6) | 10 (34.5) |
| Functional scales | | | |
| Sexual activity | 15 (51.7) | 18 (62.1) | 8 (27.6) |
| Sexual functioning | 4 (13.8) | 2 (6.9) | 2 (6.9) |

Abbreviations: EORTC, European Organisation for Research and Treatment of Cancer; QLQ-C30, general quality of life questionnaire; QLQ-PR25, prostate-cancer specific questionnaire; RT, radiotherapy; No, number; m, months.

TABLE S3. Detailed information on patients presented with grade 3 side-effects.

| Side-effect | IMRT | PBT |
|-----------------|--|---|
| Early GU | One patient developed grade 3 pelvic pain 3 months after IMRT. The pain was first associated with the initial RT-induced cystitis and recorded with grade 3 because of the use of fentanyl patch. The symptoms were then most likely associated with arthrosis. | One patient presented with grade 3 obstructive symptoms and a grade 2 urinary urgency, which were associated with an increased urinary frequency of grade 3. Therefore, a bladder catheter was inserted during the treatment. The symptoms improved at the end of the treatment and the catheter could be removed. The obstructive symptoms persisted, but an improvement was achieved with the administration of alpha-blockers. |
| Early GI | No grade 3 side-effects | At the third treatment week, one patient showed grade 3 diarrhoea that improved after oral therapy. The same patient had episodic grade 1-2 diarrhoea until the end of the therapy and mild diarrhoea 3 months afterwards, followed by no further episodes in the long-term follow up. |
| Late GU | One patient with initial stage cT4 (infiltration of the bladder) presented with grade 3 obstructive symptoms around 11 months after IMRT. He was hospitalized due to a urethra stenosis and subsequently underwent to a surgical procedure of urethral expansion with improvement of the symptoms. | No grade 3 side-effects |
| Late GI | No grade 3 side-effects | One patient had grade 2 proctitis in combination with grade 3 rectal bleeding and was hospitalized. At the same time, the patient also had a pulmonary embolism that was originally assessed as tumor-related. Subsequently, the patient received a rectoscopy and argon-plasma coagulation therapy. Afterwards, the pulmonary embolism was associated with previous circulatory diseases and treated with medical therapy. Since hospitalization was associated with both pulmonary embolism and proctitis, this toxicity was initially recorded with grade 3. |

Abbreviations: IMRT, intensity-modulated radiotherapy; GI, gastrointestinal; GU, genitourinary; PBT, proton beam therapy.

TABLE S4. Comparison of dose-volume parameter (mean \pm standard deviation) of organs at risk for patients treated with proton beam therapy (PBT) and intensity-modulated radiotherapy (IMRT).

| | D2% in Gy | D _{mean} in Gy | V40Gy (%) | V50Gy (%) | V60Gy (%) | V70Gy (%) | V75Gy (%) |
|-------------------------------|-----------------|-------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Rectum | | | | | | | |
| PBT | 74.8 \pm 1.2 | 21.1 \pm 5.0 | 27.1 \pm 7.4 | 22.7 \pm 6.5 | 15.9 \pm 4.3 | 9.4 \pm 3.0 | 2.5 \pm 2.7 |
| IMRT | 76.0 \pm 1.3 | 44.7 \pm 4.9 | 55.8 \pm 11.0 | 41.9 \pm 10.5 | 28.3 \pm 9.0 | 12.7 \pm 5.1 | 5.0 \pm 3.2 |
| p-value* | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | 0.013 | 0.005 |
| Rectal wall | | | | | | | |
| PBT | 75.3 \pm 1 | 19.7 \pm 3.4 | 25.8 \pm 4.7 | 23.1 \pm 4.2 | 18.3 \pm 3.4 | 13.6 \pm 2.8 | 4.2 \pm 4.4 |
| IMRT | 76.7 \pm 1.3 | 42 \pm 5.4 | 47.8 \pm 9.6 | 38.5 \pm 8.3 | 29.5 \pm 7.2 | 20.1 \pm 5.8 | 11.1 \pm 6.5 |
| p-value* | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |
| Bladder | | | | | | | |
| PBT | 74.8 \pm 1.3 | 20.9 \pm 10.2 | 30.0 \pm 14.0 | 20.0 \pm 13.1 | 20.0 \pm 11.6 | 10 \pm 9.1 | 0.0 \pm 6.3 |
| IMRT | 78.1 \pm 1.7 | 36.2 \pm 9.9 | 43.0 \pm 15.7 | 33.7 \pm 13.0 | 25.6 \pm 10.7 | 17.5 \pm 8.2 | 11.6 \pm 7.4 |
| p-value* | <0.001 | <0.001 | <0.001 | 0.001 | <0.002 | <0.001 | <0.001 |
| Bladder wall | | | | | | | |
| PBT | 75.3 \pm 1 | 23.3 \pm 7.9 | 30.9 \pm 10.8 | 27.7 \pm 10.0 | 23.1 \pm 8.6 | 17 \pm 6.6 | 4.7 \pm 6.6 |
| IMRT | 78.5 \pm 1.5 | 35.7 \pm 8.2 | 42.1 \pm 11.9 | 34.6 \pm 9.9 | 28.1 \pm 8.6 | 21.4 \pm 6.9 | 15.8 \pm 7.6 |
| p-value* | <0.001 | <0.001 | <0.001 | 0.006 | 0.016 | 0.010 | <0.001 |
| Bladder wall anterior | | | | | | | |
| PBT | 60.2 \pm 16.7 | 7.8 \pm 6.2 | 8.7 \pm 8.1 | 6.7 \pm 7.2 | 4.7 \pm 5.8 | 2.5 \pm 4.2 | 0.7 \pm 2.3 |
| IMRT | 74 \pm 5.2 | 24.2 \pm 7.3 | 23.6 \pm 10.1 | 15 \pm 7.3 | 9.9 \pm 6.2 | 6.0 \pm 5.0 | 3.7 \pm 4.1 |
| p-value* | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |
| Bladder wall posterior | | | | | | | |
| PBT | 75.7 \pm 1.1 | 51.1 \pm 8.3 | 70.2 \pm 12.3 | 64.5 \pm 12.3 | 54.7 \pm 12.6 | 41.4 \pm 11.4 | 11.9 \pm 14.8 |
| IMRT | 78.8 \pm 1.4 | 64 \pm 6.6 | 86.4 \pm 8.9 | 81.3 \pm 10.5 | 72.0 \pm 14.6 | 59.0 \pm 16.8 | 44.0 \pm 19.5 |
| p-value* | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |

Abbreviations: VxGy, relative volume receiving x Gy, Dx% dose to x % of organ volume, *Mann-Whitney U test

TABLE S5. Comparison of dose-volume parameter (mean \pm standard deviation) of organs at risk for patients treated with proton beam therapy (PBT) and intensity-modulated radiotherapy (IMRT) for all plans after rescaling to 74 Gy.

| | D2% in Gy | D _{mean} in Gy | V40Gy (%) | V50Gy (%) | V60Gy (%) | V70Gy (%) | V75Gy (%) |
|-------------------------------|-----------------|-------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Rectum | | | | | | | |
| PBT | 74.8 \pm 1.2 | 21.1 \pm 5.0 | 27.1 \pm 7.4 | 22.7 \pm 6.5 | 15.9 \pm 4.3 | 9.4 \pm 3.0 | 2.5 \pm 2.7 |
| IMRT | 72.8 \pm 0.6 | 42.9 \pm 4.5 | 53.3 \pm 10.8 | 39.2 \pm 10.1 | 24.2 \pm 8.0 | 8.5 \pm 2.8 | 0.0 \pm 0.1 |
| p-value* | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | 0.266 | <0.001 |
| Rectal wall | | | | | | | |
| PBT | 75.3 \pm 1.0 | 19.7 \pm 3.4 | 25.8 \pm 4.7 | 23.1 \pm 4.2 | 18.3 \pm 3.4 | 13.6 \pm 2.8 | 4.2 \pm 4.4 |
| IMRT | 73.4 \pm 0.6 | 40.3 \pm 5.1 | 46.2 \pm 9.2 | 36.7 \pm 8.1 | 27.0 \pm 6.9 | 16.7 \pm 4.8 | 0.1 \pm 0.2 |
| p-value* | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | 0.009 | <0.001 |
| Bladder | | | | | | | |
| PBT | 74.8 \pm 1.3 | 20.9 \pm 10.2 | 26.8 \pm 14.0 | 22.9 \pm 13.1 | 18.0 \pm 11.6 | 11.7 \pm 9.1 | 3.0 \pm 6.3 |
| IMRT | 74.8 \pm 0.8 | 34.7 \pm 9.2 | 41.2 \pm 15.1 | 31.8 \pm 12.2 | 23.2 \pm 9.8 | 14.6 \pm 6.9 | 2.4 \pm 2.5 |
| p-value* | 0.35 | <0.001 | <0.001 | 0.003 | 0.012 | 0.027 | 0.18 |
| Bladder wall | | | | | | | |
| PBT | 75.3 \pm 1.0 | 23.3 \pm 7.9 | 30.9 \pm 10.8 | 27.7 \pm 10.0 | 23.1 \pm 8.6 | 17.0 \pm 6.6 | 4.7 \pm 6.6 |
| IMRT | 75.2 \pm 0.5 | 34.2 \pm 7.6 | 40.7 \pm 11.4 | 33.2 \pm 9.4 | 26.1 \pm 7.9 | 19.1 \pm 6.1 | 3.9 \pm 3.2 |
| p-value* | 0.387 | <0.001 | 0.001 | 0.009 | 0.038 | 0.074 | 0.20 |
| Bladder wall anterior | | | | | | | |
| PBT | 60.2 \pm 16.7 | 7.8 \pm 6.2 | 8.7 \pm 8.1 | 6.7 \pm 7.2 | 4.7 \pm 5.8 | 2.5 \pm 4.2 | 0.7 \pm 2.3 |
| IMRT | 70.9 \pm 4.6 | 23.2 \pm 6.9 | 21.8 \pm 9.4 | 13.6 \pm 7.0 | 8.7 \pm 5.8 | 4.9 \pm 4.6 | 0.9 \pm 1.7 |
| p-value* | 0.003 | <0.001 | <0.001 | <0.001 | <0.001 | 0.004 | 0.030 |
| Bladder wall posterior | | | | | | | |
| PBT | 75.7 \pm 1.1 | 51.1 \pm 8.3 | 70.2 \pm 12.3 | 64.5 \pm 12.3 | 54.7 \pm 12.6 | 41.4 \pm 11.4 | 11.9 \pm 14.8 |
| IMRT | 75.5 \pm 0.5 | 61.3 \pm 6.3 | 85.6 \pm 9.1 | 79.9 \pm 11.1 | 68.3 \pm 15.9 | 54.4 \pm 17.1 | 10.8 \pm 8.9 |
| p-value* | 0.69 | <0.001 | <0.001 | <0.001 | 0.002 | 0.007 | 0.35 |

Abbreviations: VxGy, relative volume receiving x Gy, Dx% dose to x % of organ volume, *Mann-Whitney U test

TABLE S6. Baseline Quality of Life Scores according to EORTC QLQ-C30 and prostate-cancer specific QLQ-PR25 module.

| Item | IMRT | | | PBT | | |
|------------------------------------|-----------------|--------|---------------|-----------------|--------|---------------|
| | Mean \pm SD | Median | IQR | Mean \pm SD | Median | IQR |
| EORTC QLQ-C30 | | | | | | |
| Global health status | 61.9 \pm 24.1 | 66.7 | [50 - 83.3] | 73.0 \pm 21.3 | 83.3 | [66.7 - 83.3] |
| Role functioning | 80.3 \pm 25.9 | 91.7 | [70.8 - 100] | 93.2 \pm 18.6 | 100.0 | [100 - 100] |
| Emotional functioning | 76.5 \pm 24.2 | 79.2 | [66.7 - 100] | 67.0 \pm 29.8 | 75.0 | [41.7 - 91.7] |
| Physical functioning | 80.3 \pm 18.8 | 80.0 | [70 - 96.7] | 88.7 \pm 18.3 | 100.0 | [83.3 - 100] |
| Social functioning | 84.8 \pm 21.9 | 100.0 | [70.8 - 100] | 81.1 \pm 27.7 | 83.3 | [83.3 - 100] |
| Cognitive functioning | 81.1 \pm 20.3 | 83.3 | [66.7 - 100] | 84.1 \pm 17.0 | 83.3 | [83.3 - 100] |
| Pain | 21.3 \pm 25.3 | 0.0 | [0 - 45.8] | 14.8 \pm 27.7 | 0.0 | [0 - 16.7] |
| Diarrhoea | 6.1 \pm 12.9 | 0.0 | [0 - 0] | 6.1 \pm 12.9 | 0.0 | [0 - 0] |
| Fatigue | 26.8 \pm 27.6 | 22.2 | [0 - 41.7] | 25.0 \pm 21.8 | 22.2 | [11.1 - 30.6] |
| Insomnia | 21.2 \pm 27.6 | 0.0 | [0 - 33.3] | 27.3 \pm 29.5 | 33.3 | [0 - 33.3] |
| Constipation | 9.1 \pm 22.9 | 0.0 | [0 - 0] | 6.1 \pm 12.9 | 0.0 | [0 - 0] |
| Nausea and vomiting | 0 \pm 0 | 0.0 | [0 - 0] | 0.8 \pm 3.5 | 0.0 | [0 - 0] |
| Appetite loss | 7.9 \pm 17.5 | 0.0 | [0 - 0] | 6.3 \pm 22.1 | 0.0 | [0 - 0] |
| Dyspnoea | 12.1 \pm 25.7 | 0.0 | [0 - 0] | 10.6 \pm 18.5 | 0.0 | [0 - 25] |
| Financial difficulties | 10.6 \pm 21 | 0.0 | [0 - 0] | 4.5 \pm 20.8 | 0.0 | [0 - 0] |
| EORTC QLQ-PR25 | | | | | | |
| Urinary symptoms | 24 \pm 14.4 | 19.0 | [19 - 28.6] | 24.4 \pm 17.2 | 21.4 | [12.9 - 34.5] |
| Incontinence aid | 6.1 \pm 12.9 | 0.0 | [0 - 0] | 9.1 \pm 20.6 | 0.0 | [0 - 0] |
| Bowel symptoms | 4.2 \pm 8 | 0.0 | [0 - 2.1] | 2.8 \pm 7.1 | 0.0 | [0 - 0] |
| Hormone treatment-related symptoms | 9.3 \pm 12 | 0.0 | [0 - 17.8] | 8.5 \pm 13.4 | 0.0 | [0 - 14.4] |
| Sexual activity | 65.6 \pm 30.1 | 66.7 | [41.7 - 91.7] | 62.2 \pm 29.5 | 66.7 | [41.7 - 91.7] |
| Sexual functioning | 50.7 \pm 9.7 | 47.2 | [43.8 - 54.2] | 60.4 \pm 20.7 | 70.8 | [56.3 - 75] |

Abbreviations: SD, standard deviation; IQR, interquartile range; PBRT, proton beam therapy; IMRT, intensity-modulated radiotherapy.

TABLE S7. Quality of Life Scores according to EORTC QLQ-C30 and prostate-cancer specific QLQ-PR25 3 months after radiotherapy.

| Item | IMRT | | | PBT | | |
|------------------------------------|-----------------|--------|---------------|-----------------|--------|---------------|
| | Mean \pm SD | Median | IQR | Mean \pm SD | Median | IQR |
| Global health status | 69.4 \pm 16.2 | 66.7 | [50 - 83.3] | 68.5 \pm 24.6 | 79.2 | [60.4 - 83.3] |
| Role functioning | 86.3 \pm 21.6 | 100.0 | [83.3 - 100] | 86.3 \pm 23 | 100.0 | [83.3 - 100] |
| Emotional functioning | 81.9 \pm 24.9 | 91.7 | [75 - 100] | 78.7 \pm 27.8 | 91.7 | [56.3 - 100] |
| Physical functioning | 82.5 \pm 14.7 | 86.7 | [70 - 93.3] | 88.4 \pm 16.3 | 93.3 | [86.7 - 100] |
| Social functioning | 85.3 \pm 20.5 | 100.0 | [66.7 - 100] | 88.2 \pm 19.6 | 100.0 | [83.3 - 100] |
| Cognitive functioning | 88 \pm 13.4 | 83.3 | [83.3 - 100] | 81.5 \pm 24.8 | 83.3 | [70.8 - 100] |
| Pain | 16.7 \pm 25.6 | 0.0 | [0 - 16.7] | 15.7 \pm 26.5 | 0.0 | [0 - 33.3] |
| Diarrhoea | 7.4 \pm 13.9 | 0.0 | [0 - 0] | 11.1 \pm 22.2 | 0.0 | [0 - 0] |
| Fatigue | 29.5 \pm 22.5 | 33.3 | [11.1 - 44.4] | 26.3 \pm 30 | 22.2 | [0 - 38.9] |
| Insomnia | 28.1 \pm 31.1 | 33.3 | [0 - 50] | 31.6 \pm 31.5 | 33.3 | [0 - 33.3] |
| Constipation | 20.4 \pm 31.7 | 0.0 | [0 - 33.3] | 3.7 \pm 10.5 | 0.0 | [0 - 0] |
| Nausea and vomiting | 1.8 \pm 5.1 | 0.0 | [0 - 0] | 2.6 \pm 8.1 | 0.0 | [0 - 0] |
| Appetite loss | 7 \pm 17.4 | 0.0 | [0 - 0] | 3.5 \pm 14.9 | 0.0 | [0 - 0] |
| Dyspnoea | 10.5 \pm 18.9 | 0.0 | [0 - 16.7] | 12.3 \pm 27 | 0.0 | [0 - 0] |
| Financial difficulties | 7.4 \pm 13.9 | 0.0 | [0 - 0] | 11.1 \pm 24.8 | 0.0 | [0 - 0] |
| Urinary symptoms | 32.5 \pm 18.7 | 28.6 | [23.8 - 45.2] | 28.4 \pm 17 | 23.8 | [14.3 - 38.1] |
| Incontinence aid | 20.8 \pm 20 | 33.3 | [0 - 33.3] | 12.5 \pm 16.1 | 0.0 | [0 - 33.3] |
| Bowel symptoms | 11.8 \pm 18.3 | 8.3 | [0 - 16.7] | 5.4 \pm 7 | 0.0 | [0 - 8.3] |
| Hormone treatment-related symptoms | 17 \pm 15.4 | 13.3 | [6.7 - 26.7] | 16.9 \pm 18.3 | 13.3 | [0 - 20] |
| Sexual activity | 76.9 \pm 26.1 | 83.3 | [66.7 - 100] | 70.4 \pm 27.5 | 66.7 | [50 - 100] |
| Sexual functioning | 41.7 \pm 0 | 41.7 | [41.7 - 41.7] | 70.8 \pm 4.2 | 70.8 | [68.8 - 72.9] |

Abbreviations: SD, standard deviation; IQR, interquartile range; PBRT, proton beam therapy; IMRT, intensity-modulated radiotherapy.

TABLE S8. Quality of Life Scores according to EORTC QLQ-C30 and prostate-cancer specific QLQ-PR25 12 months after radiotherapy.

| Item | IMRT | | | PBT | | |
|------------------------------------|-----------------|--------|---------------|-----------------|--------|---------------|
| | Mean \pm SD | Median | IQR | Mean \pm SD | Median | IQR |
| EORTC QLQ-C30 | | | | | | |
| Global health status | 67.4 \pm 20.2 | 66.7 | [58.3 - 83.3] | 74.2 \pm 20.9 | 83.3 | [62.5 - 83.3] |
| Role functioning | 70 \pm 25.6 | 66.7 | [54.2 - 95.8] | 85 \pm 21.7 | 100.0 | [70.8 - 100] |
| Emotional functioning | 64.4 \pm 25.6 | 58.3 | [41.7 - 87.5] | 81.1 \pm 29.5 | 100.0 | [70.8 - 100] |
| Physical functioning | 73.3 \pm 20.9 | 73.3 | [63.3 - 93.3] | 86.7 \pm 18.2 | 100.0 | [76.7 - 100] |
| Social functioning | 76.7 \pm 22.6 | 75.0 | [66.7 - 100] | 90 \pm 17 | 100.0 | [87.5 - 100] |
| Cognitive functioning | 78.3 \pm 23.6 | 91.7 | [50 - 100] | 85 \pm 29.3 | 100.0 | [83.3 - 100] |
| Pain | 30.3 \pm 32.4 | 33.3 | [0 - 33.3] | 21.2 \pm 28.5 | 0.0 | [0 - 33.3] |
| Diarrhoea | 10 \pm 15.3 | 0.0 | [0 - 25] | 10 \pm 21.3 | 0.0 | [0 - 0] |
| Fatigue | 35.4 \pm 28 | 44.4 | [5.6 - 50] | 28.3 \pm 25.2 | 22.2 | [5.6 - 38.9] |
| Insomnia | 30.3 \pm 33.2 | 33.3 | [0 - 50] | 33.3 \pm 37.6 | 33.3 | [0 - 50] |
| Constipation | 23.3 \pm 30 | 16.7 | [0 - 33.3] | 13.3 \pm 22.1 | 0.0 | [0 - 25] |
| Nausea and vomiting | 3 \pm 6.4 | 0.0 | [0 - 0] | 4.5 \pm 10.3 | 0.0 | [0 - 0] |
| Appetite loss | 12.1 \pm 16 | 0.0 | [0 - 33.3] | 9.1 \pm 20.6 | 0.0 | [0 - 0] |
| Dyspnoea | 6.1 \pm 12.9 | 0.0 | [0 - 0] | 18.2 \pm 26.1 | 0.0 | [0 - 33.3] |
| Financial difficulties | 24.2 \pm 32.1 | 0.0 | [0 - 33.3] | 9.1 \pm 20.6 | 0.0 | [0 - 0] |
| EORTC QLQ-PR25 | | | | | | |
| Urinary symptoms | 36.4 \pm 19 | 33.3 | [23.8 - 57.1] | 35.9 \pm 23.3 | 42.9 | [14.3 - 52.4] |
| Incontinence aid | 15.2 \pm 16.6 | 0.0 | [0 - 33.3] | 30.3 \pm 36.1 | 0.0 | [0 - 66.7] |
| Bowel symptoms | 17.5 \pm 16.4 | 20.8 | [0 - 25] | 16.7 \pm 19 | 12.5 | [2.1 - 22.9] |
| Hormone treatment-related symptoms | 20.3 \pm 22.9 | 16.7 | [0 - 26.7] | 11.7 \pm 14.9 | 6.7 | [0 - 18.3] |
| Sexual activity | 75 \pm 26.4 | 83.3 | [58.3 - 100] | 54.2 \pm 28.6 | 33.3 | [33.3 - 75] |
| Sexual functioning | 58.3 \pm 8.3 | 58.3 | [54.2 - 62.5] | 62.5 \pm 4.2 | 62.5 | [60.4 - 64.6] |

Abbreviations: SD, standard deviation; IQR, interquartile range; PBRT, proton beam therapy; IMRT, intensity-modulated radiotherapy.

TABLE S9. Comparison of results of the present study and a study by Gray et al. [1] regarding quality of life symptoms in bowel and urinary domains. At the top of the table, baseline values are given. Below, differences at 3 and 12 months after treatment compared to the baseline values are presented. On the right side, these changes are compared between IMRT and PBT for the present study.

| Questionnaire | Study by Gray et al. [1] | | | | | | | | Present study | | | | | | | | | |
|--------------------|---------------------------------|------|----------------------|---------------------|---------------------------------|------|----------------------|---------------------|---------------------------------|------|----------------------|---------------------|---------------------------------|------|----------------------|---------------------|------------------------------------|--|
| | PBT | | | | IMRT | | | | PBT | | | | IMRT | | | | | |
| | PCSI* | | | | EPIC | | | | EORTC-QLQ-PR25* | | | | EORTC-QLQ-PR25* | | | | | |
| | Mean Score | | SD | | Mean Score | | SD | | Mean Score | | SD | | Mean Score | | SD | | | |
| Baseline | | | | | | | | | | | | | | | | | | |
| Bowel symptoms | 95.1 | 6.7 | | | 94.3 | 10.9 | | | 97.2 | 7.1 | | | 95.8 | 8.0 | | | | |
| Urinary symptoms | 78.4 | 11.0 | | | 86.4 | 14.4 | | | 75.6 | 17.2 | | | 76.0 | 14.4 | | | | |
| | Mean score change from baseline | | SD | | Mean score change from baseline | | SD | | Mean score change from baseline | | SD | | Mean score change from baseline | | SD | | | |
| | | | p-value [†] | Mean change >0.5 SD | | | p-value [†] | Mean change >0.5 SD | | | p-value [†] | Mean change >0.5 SD | | | p-value [†] | Mean change >0.5 SD | p-value [#] (IMRT vs PBT) | |
| 3 months after RT | | | | | | | | | | | | | | | | | | |
| Bowel symptoms | -1.7 | 8.3 | 0.062 | - | -16.0 | 21.4 | <0.001 | + | -4.8 | 9.5 | 0.19 | + | -9.5 | 12.2 | 0.068 | + | 0.30 | |
| Urinary symptoms | -4.8 | 13.8 | 0.002 | - | -16.5 | 19.9 | <0.001 | + | -4.7 | 15.2 | 0.29 | - | -11.9 | 16.9 | 0.012 | + | 0.09 | |
| 12 months after RT | | | | | | | | | | | | | | | | | | |
| Bowel symptoms | -6.4 | 13.2 | <0.001 | + | -6.3 | 16.2 | <0.001 | + | -25.0 | 29.7 | 0.11 | + | -16.7 | 20.4 | 0.18 | + | 0.38 | |
| Urinary symptoms | -6.0 | 16.9 | 0.002 | + | 0.9 | 15.8 | 0.52 | - | -9.1 | 19.6 | 0.26 | + | -16.0 | 19.8 | 0.036 | + | 0.19 | |

Abbreviations: EORTC-QLQ-PR25, prostate-cancer specific questionnaire from the European Organisation for Research and Treatment of Cancer; EPIC, Expanded Prostate Cancer Index Composite; IMRT, intensity-modulated radiotherapy; PBT, proton beam therapy; PCSI, Prostate Cancer Symptom Indices; RT, radiotherapy; SD, standard deviation

* The PCSI and EORTC symptom scales were inverted so that low values represent low symptoms on a linear scale ranging from 0 to 100. Thus, the three instruments are comparable.

[†] paired t-test

[‡] Wilcoxon test

[#] Mann-Whitney U test

[1] Gray PJ, Paly JJ, Yeap BY, et al. Patient-Reported Outcomes After 3-Dimensional Conformal, Intensity-Modulated, or Proton Beam Radiotherapy for Localized Prostate Cancer. *Cancer* 2013;119:10.1002/cncr.27956

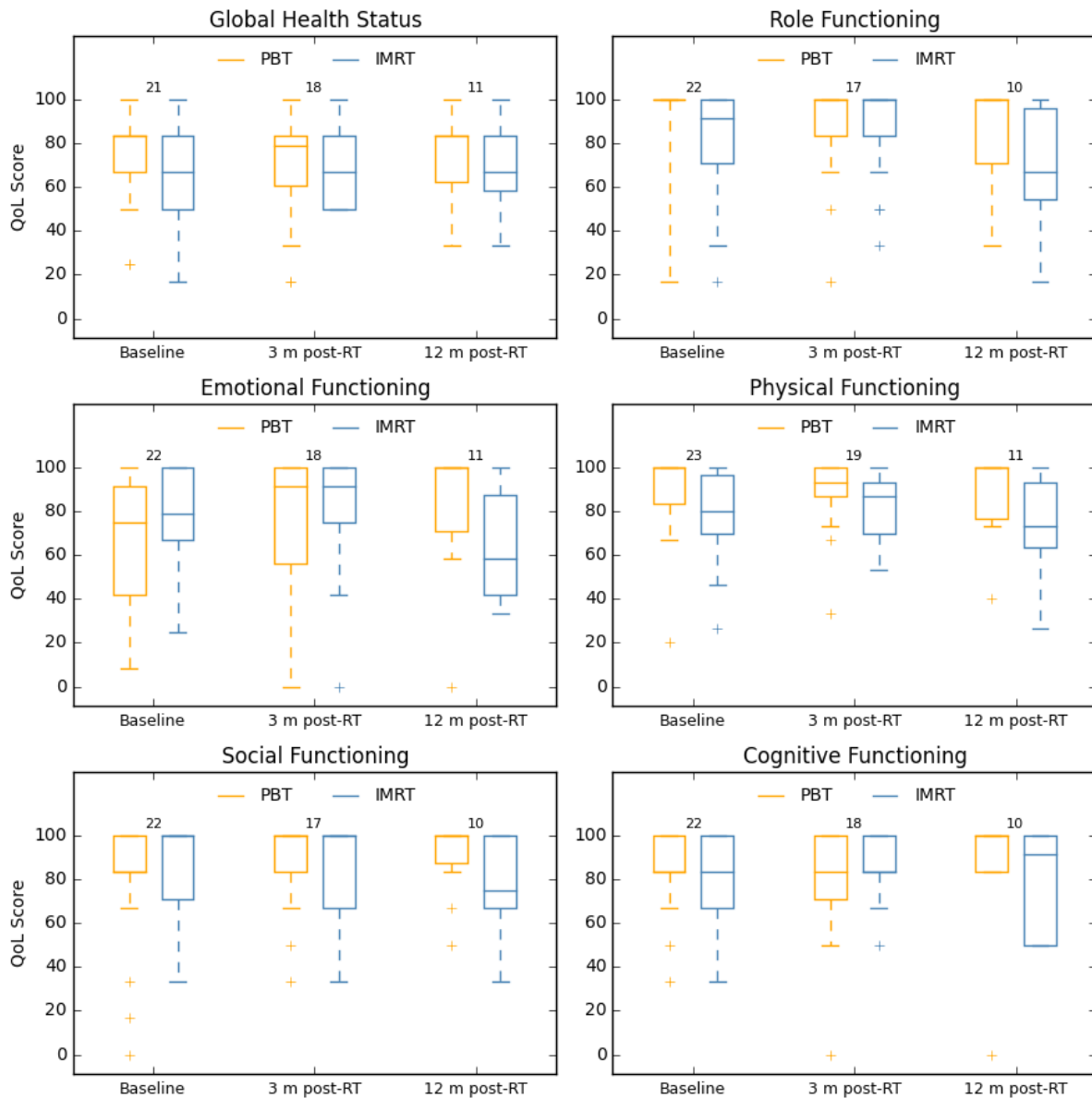


Figure S1. Development of absolute quality of life (QoL) scores of the EORTC-C30 items on the functional scale. High scores represent high/healthy level of functioning or global health status. Numbers above the boxplots represent the number of complete pairs at this time point. RT, radiotherapy; m, months.

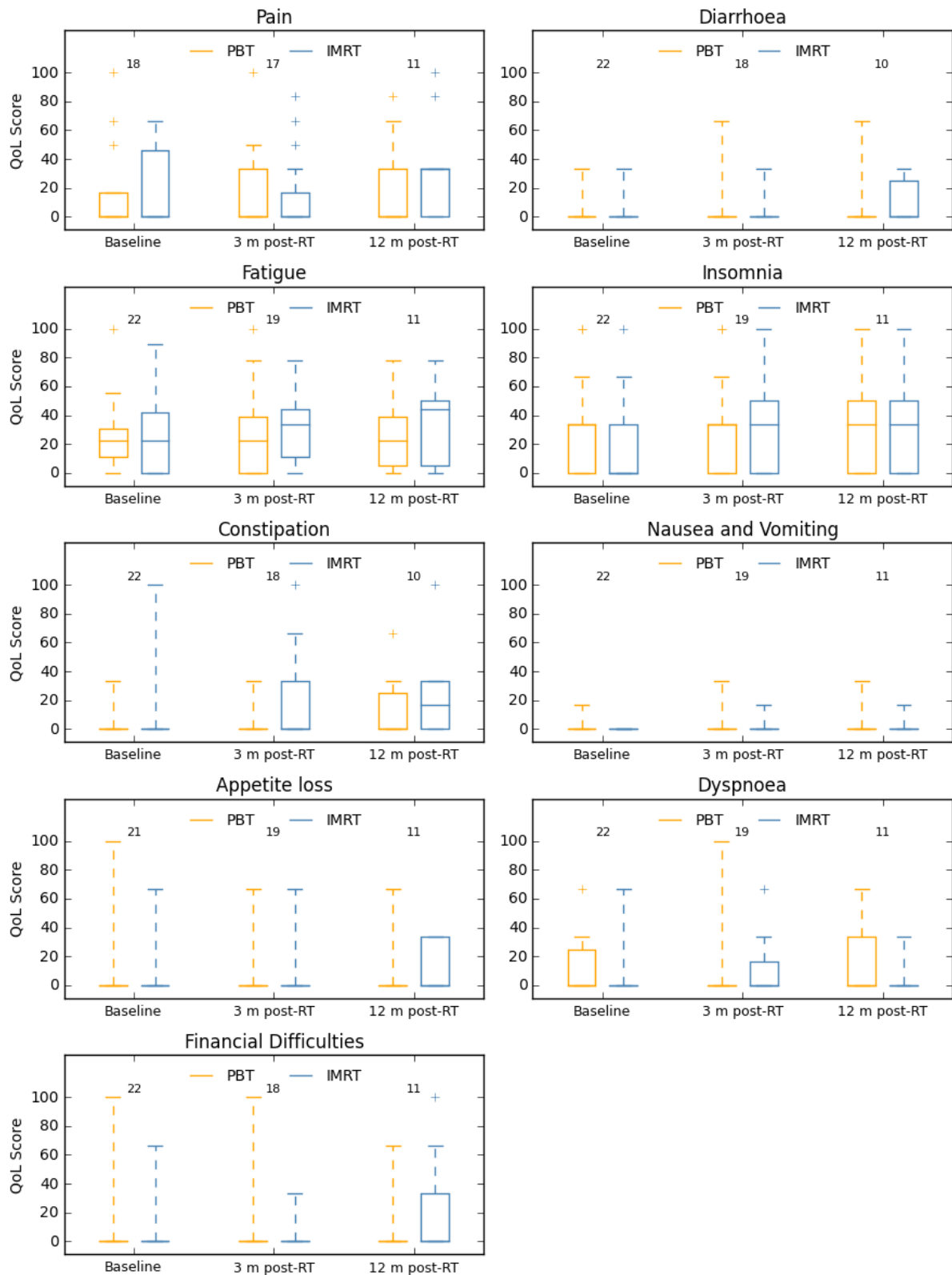


Figure S2. Development of absolute quality of life (QoL) scores of the EORTC-C30 items on the symptom scale. High scores represent high level of symptomatology or problems. Numbers above the boxplots represent the number of complete pairs at this time point. RT, radiotherapy; m, months.

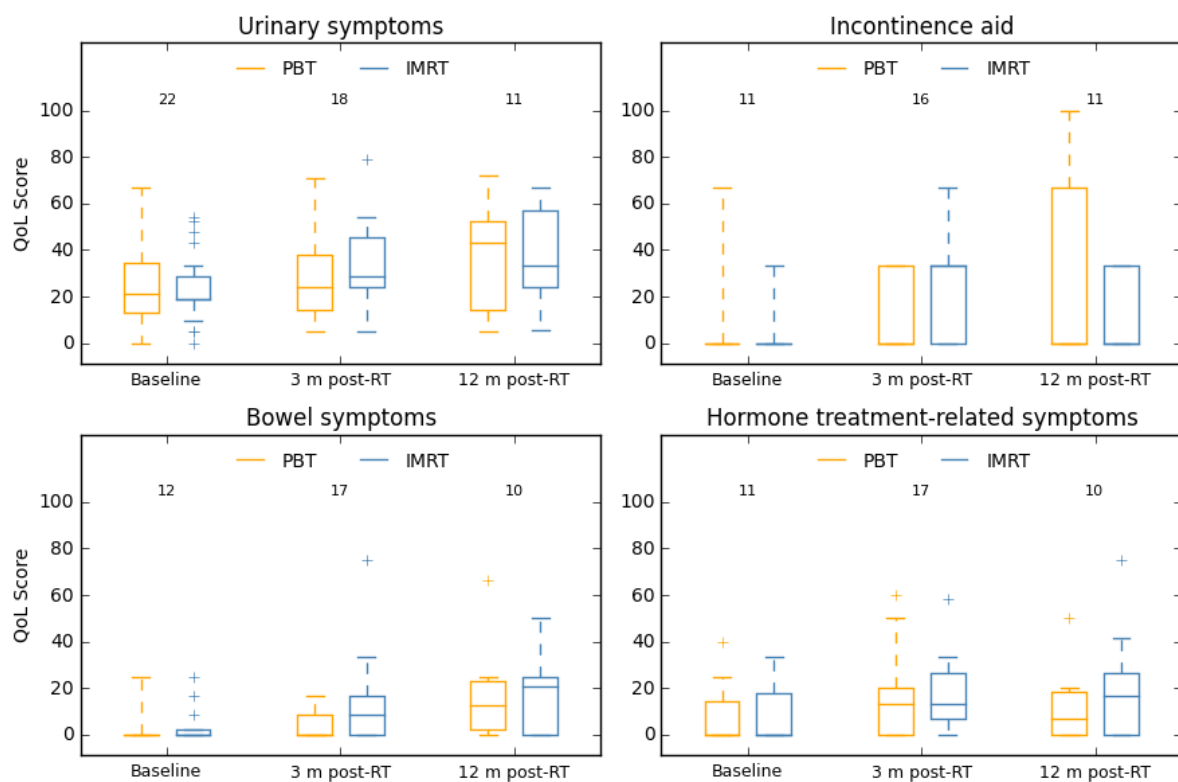


Figure S3. Development of absolute quality of life (QoL) scores of the prostate-cancer specific EORTC-PR25 items on the symptom scale. High scores represent high level of symptomatology or problems. Numbers above the boxplots represent the number of complete pairs at this time point. RT, radiotherapy; m, months.

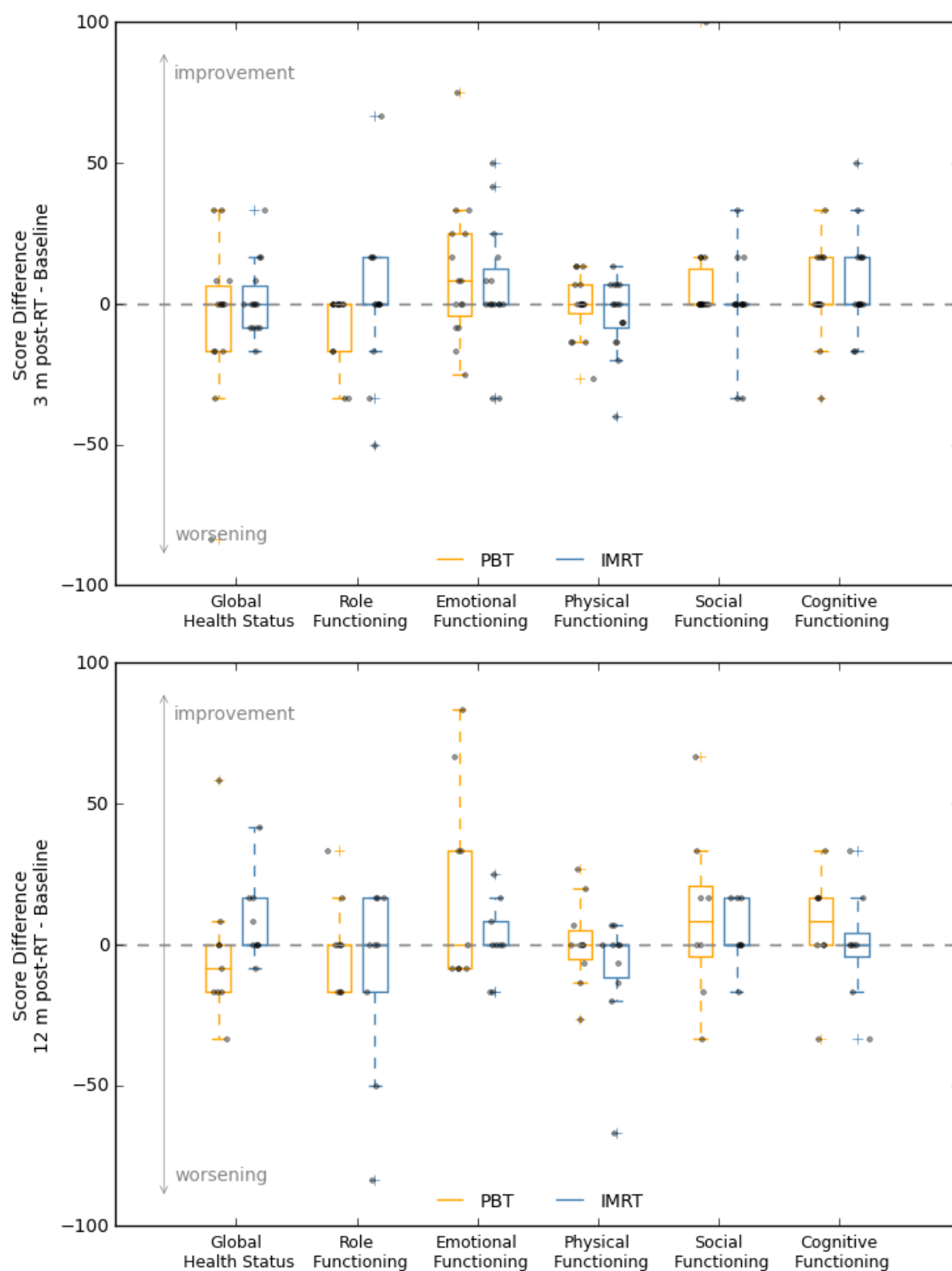


Figure S4. Differences in the absolute quality of life (QoL) scores of the EORTC-C30 items on the functional scale between scores 3 months (3 m, top) and 12 months (12 m, bottom) after radiotherapy (RT) and at baseline. Positive score differences represent an improvement in functioning or global health status. Each patient is represented by a gray dot.

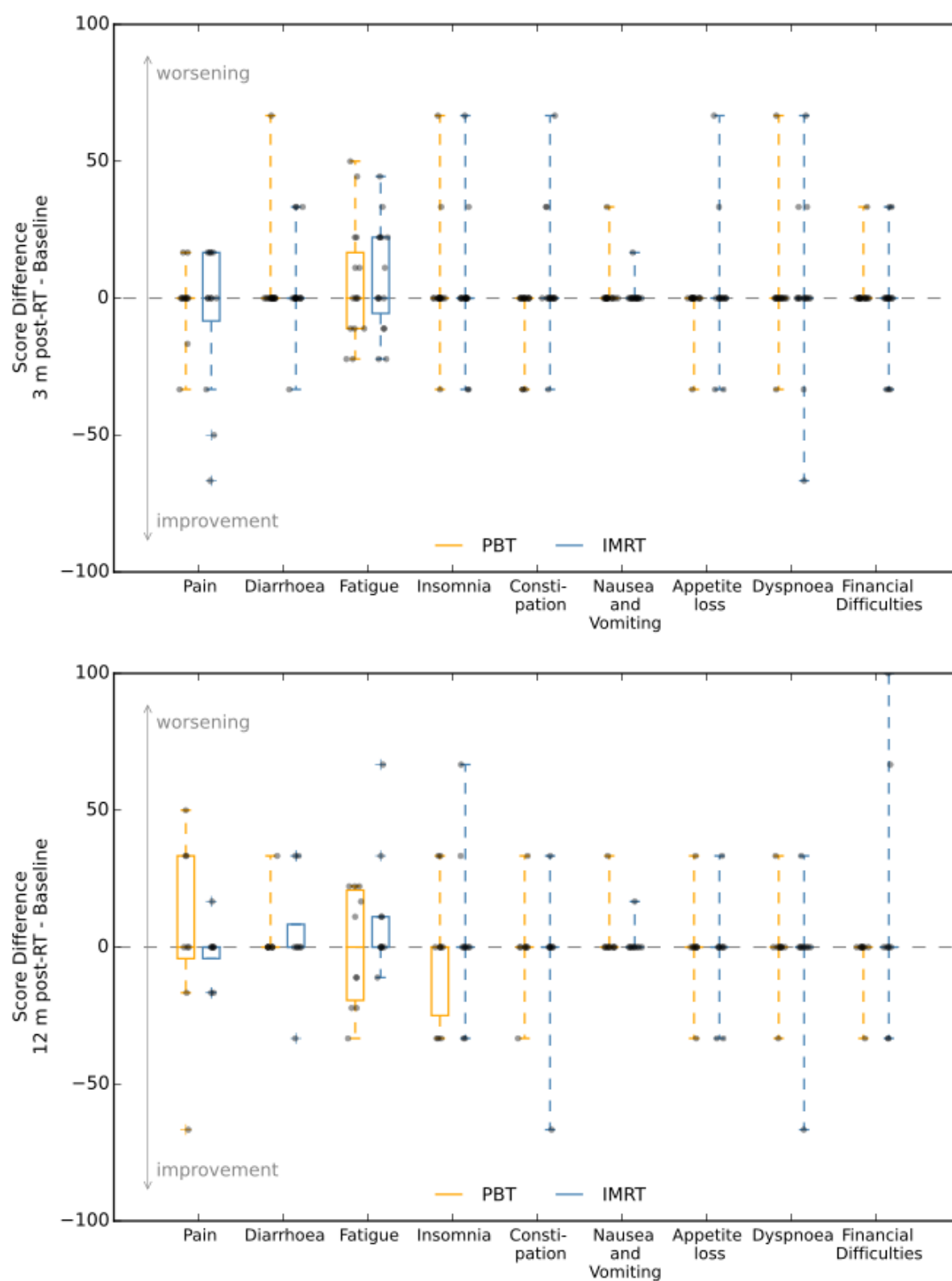


Figure S5. Differences in the absolute quality of life (QoL) scores of the EORTC-C30 items on the symptom scale between scores 3 months (3 m, top) and 12 months (12 m, bottom) after radiotherapy (RT) and at baseline. Positive score differences represent a worsening in symptomatology. Each patient is represented by a gray dot.

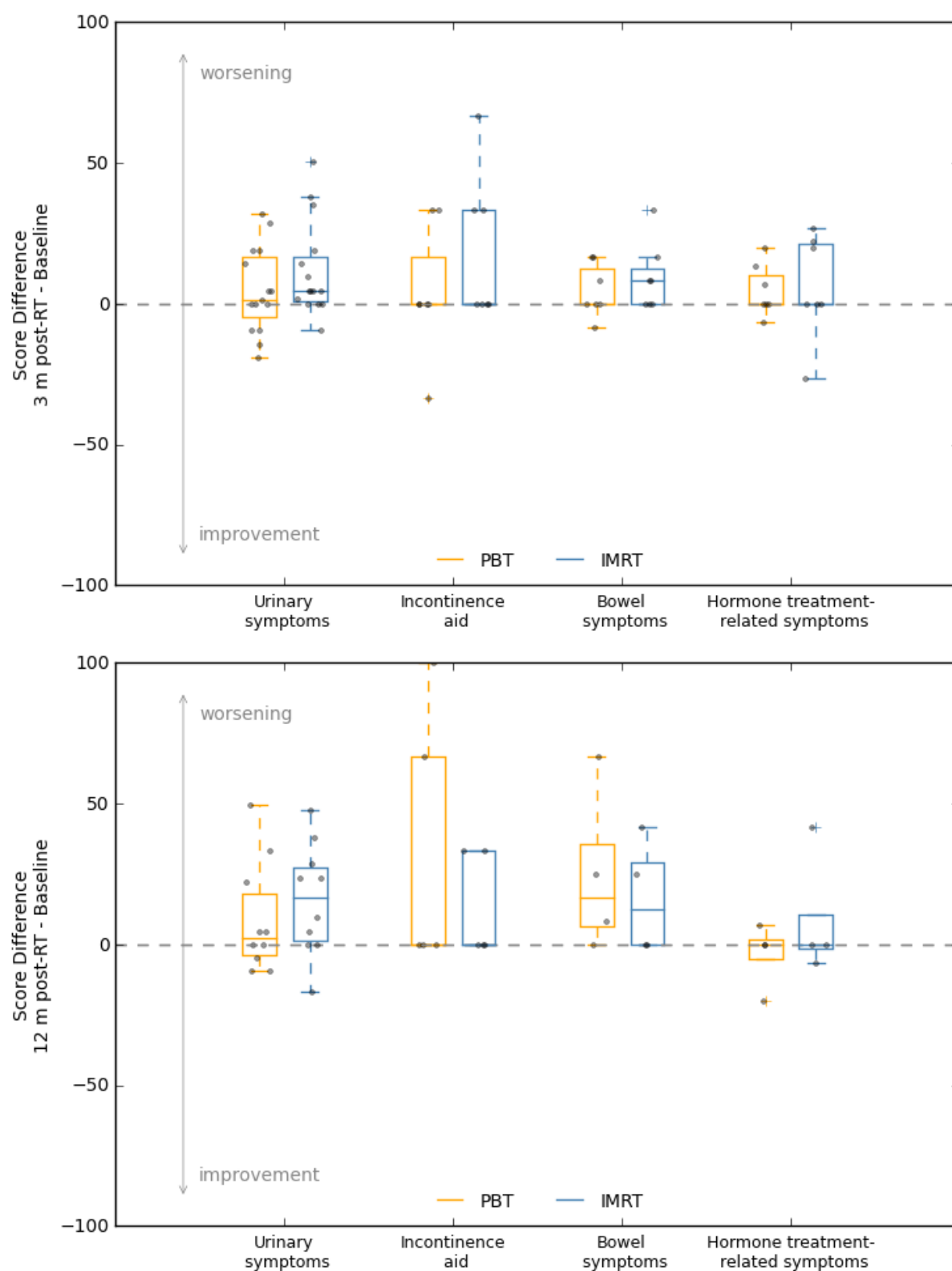


Figure S6. Differences in the absolute quality of life (QoL) scores of the EORTC-PR25 items on the symptom scale between scores 3 months (3 m, top) and 12 months (12 m, bottom) after radiotherapy (RT) and at baseline. Positive score differences represent a worsening in symptomatology. Each patient is represented by a gray dot.