Real-world utilisation of brachytherapy boost and patient-reported functional outcomes in men who had external beam radiation therapy for prostate cancer in Australia

Wee Loon Ong a,b,c,⁎, Melanie Evans d , Nathan Papa d , Jeremy Millar a,b,d

a Alfred Health Radiation Oncology, Melbourne VIC, Australia
b Central Clinical School, Monash University, Melbourne, VIC, Australia
c Department of Radiation Oncology, Odette Cancer Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, ON, Canada
d School of Public Health and Preventive Medicine, Monash University, Melbourne VIC, Australia

ARTICLE INFO

Keywords:
Prostate Cancer
Brachytherapy
Registry
Patient-reported outcomes

ABSTRACT

Background and purpose: We aimed to evaluate utilisation of brachytherapy (BT) boost in men who had external beam radiation therapy (EBRT) for prostate cancer, and to compare patient-reported functional outcomes (PRO) following each approach in a population-based setting in Australia.

Materials and methods: This is a population-based cohort of men with localised prostate cancer enrolled in the Victorian Prostate Cancer Outcomes Registry, who had EBRT between 2015 and 2020. Primary outcomes were proportion who had BT-boost, and PRO (assessed using the EPIC-26 questionnaires) 12 months post-treatment. Multivariable logistic regressions were used to evaluate factors associated with BT-boost, and linear regressions were used to estimate differences in EPIC-26 domain scores between EBRT alone and EBRT + BT.

Results: Of the 1,626 men in the study, 88 (5.4 %) had BT-boost. Factors independently associated with BT-boost were younger age, higher socioeconomic status, and treatment in public institutions. 1,555 men completed EPIC-26 questionnaires. No statistically or clinically significant differences in EPIC-26 urinary, sexual and bowel functional domain scores were observed between men who had EBRT + BT vs EBRT alone, with adjusted mean differences in urinary incontinence, urinary irritative/ obstruction, sexual, and bowel domain of 1.28 (95 %CI = −3.23 to 5.79), −2.87 (95 %CI = −6.46 to 0.73), 0.49 (95 %CI = −4.78 to 5.76), and 2.89 (95 %CI = −0.83 to 6.61) respectively.

Conclusion: 1-in-20 men who had EBRT for prostate cancer had BT-boost. This is the first time that PRO following EBRT ± BT is reported at a population-based level in Australia, with no evidence to suggest worse PRO with addition of BT-boost 12 months post-treatment.

Introduction

Brachytherapy (BT) boost is an approach for dose escalation in men with prostate cancer treated with external beam radiation therapy (EBRT). BT-boost has been shown in several randomized trials to be associated with improved biochemical disease-free survival [1–4]. Recent multi-institutional pooled analyses showed BT-boost to be associated with reduced prostate cancer specific mortality and distant metastases in men with high-risk disease [5]. Notwithstanding this, population-based studies have shown that BT utilization remains low for various reasons [6–12]. Some of these include: reimbursement disincentive for BT which varies between different healthcare system in different countries, the belief that dose-escalation can be achieved with advancement in LINAC-based techniques such as stereotactic radiation therapy boost [13,14], and the decline in BT exposure during radiation oncology training, which translates into shortfall of radiation oncologist proficient in BT in the long-term [15,16].

There is also concern regarding increased risk of urinary toxicities with BT boost [17,18], with late Grade 3 urinary toxicity reported to be as high as 18 % at 5 years in the low-dose-rate (LDR) BT-boost arm in the ASCENDE-RT trials [17]. However, in the Hoskin trials, no differences in early and late urinary and bowel toxicities were reported between men who had EBRT with or without high-dose-rate (HDR) BT-boost at a median follow-up of more than 10 years, assessed using the Functional

⁎ Corresponding author at: Alfred Health Radiation Oncology, 55 Commercial Road, Melbourne 3004, VIC, Australia.
E-mail address: weeloonong@cantab.net (W.L. Ong).

https://doi.org/10.1016/j.ctro.2022.08.009
Received 5 July 2022; Received in revised form 12 August 2022; Accepted 16 August 2022
Available online 19 August 2022
2405-6308/© 2022 The Author(s). Published by Elsevier B.V. on behalf of European Society for Radiotherapy and Oncology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
Assessment of Cancer Therapy-Prostate (FACT-P) and General (FACT-G) tool [19]. The understanding of the toxicity outcomes of BT-boost is especially important in guiding patients’ treatment decision-making, given the excellent long-term oncological outcomes in prostate cancer, and the multiple curative treatment options available for men with prostate cancer [20]. While several single institutional retrospective studies [21,22] have reported on the toxicity outcomes following EBRT + BT-boost, few included patient-reported outcomes (PRO) data [23–25]. There is also extremely limited published toxicity outcomes data at population-based level [26,27].

In this study, we aim to evaluate 1) the utilisation of BT-boost in men who had EBRT for prostate cancer, and 2) the PRO following EBRT with or without BT-boost in real-life Australian population-based setting.

Methods

Study population

This is a population-based cohort of men with prostate cancer enrolled in the Victorian Prostate Cancer Outcomes Registry (PCOR-Vic), a state-wide clinical quality registry, which currently captures over 80% of incident prostate cancer cases in Victoria, the second most populous state in Australia with a population of approximately 6 million people. Detailed recruitment and data collection methodology have been previously described [28]. Briefly, all men with newly diagnosed prostate cancer were notified to PCOR-Vic, with an opt-out consent process to maximise recruitment. Trained data collectors reviewed medical records and made follow-up phone interviews with patients to verify treatment details. All men were contacted 12-months post-treatment to complete the Expanded Prostate Cancer Index Composite short form 26 questionnaire (EPIC-26), a validated PRO tool for prostate cancer [29]. The questionnaire was initially administered by phone or sent out to patients by post, but has been predominantly administered via email since April 2018, with a minority still completing the survey by phone or post. The EPIC-26 included urinary incontinence, urinary obstructive, sexual, bowel, and hormonal function domain scores, ranging from 0 to 100, with higher score representing better outcomes. Due to the nature of recruitment into PCOR-Vic, all men would have been started on treatment by the time they were enrolled in PCOR-Vic, and hence it was not possible to capture baseline EPIC-26 within PCOR-Vic. For this study, we included all men who had definitive EBRT, with or without BT-boost, as primary treatment for localised prostate cancer between 1 January 2015 and 31 December 2020.

Primary outcomes and covariables

The primary outcomes were 1) proportion of men who had BT-boost and factors associated with that, and 2) differences in EPIC-26 functional domains outcomes at 12 months post-treatment between men who had EBRT and EBRT + BT. Covariables available within PCOR-Vic include year of treatment, age at treatment, PSA level at diagnosis, ISUP grade group, clinical T categories, NCCN risk categories (low, intermediate, or high risk), use of androgen deprivation therapy (ADT), residential postcode, and treatment centres. Based on the residential postcode, the area of residence was classified as major city, inner regional, or outer regional/remote using the Australian Statistical Geographical Standard (ASGS) remoteness structure. In addition, the socioeconomic status was derived from the residential postcode using the Socio-Economic Indexes for Areas (SEIFA) index for relative socioeconomic disadvantaged based on the Australian Bureau of Statistics. This was further subdivided into quintiles based on the Victorian population. There were four public and two private radiation therapy service providers in Victoria, and each provided radiation therapy services through several treatment centres throughout Victoria. These treatment centres were classified as metropolitan or regional depending on the location of the treatment centres based on the ASGS structure. BT boosts were largely offered only in two public metropolitan centres that were equipped with HDR-BT expertise. Recognizing that men may have the EBRT and BT at separate centres, for the study purpose, the treatment institution classification (public or private, and metropolitan or regional) was based on the institution where they received EBRT.

Statistical analyses

Differences in covariables between men who had EBRT and EBRT + BT were compared using Pearson’s chi-squared test for categorical variables and Student’s t-test (or Mann-Whitney U test for expected non-normality in PSA values) for continuous variables. Multivariable logistic regression was used to evaluate association of covariables with EBRT + BT use. Covariables included in multivariable analyses were pre-selected based on clinical knowledge, and these included year of treatment, age at treatment, NCCN risk categories, ADT use, socioeconomic status, area of residence and treatment centres. Differences in the EPIC-26 domain scores between EBRT and EBRT + BT were estimated using multivariable linear regression, adjusting for available covariables. EBRT alone was the reference group, and negative differences indicated poorer outcomes compared to EBRT alone, and positive differences indicated better outcomes compared to EBRT alone. Minimally clinically important differences (MCID) in the adjusted EPIC-26 domain scores were defined based on previous study [30], i.e., 6, 5, 10, 4 and 4 for urinary incontinence, urinary obstruction, sexual, bowel and hormonal domains respectively. A two-sided P-value < 0.05 was considered to indicate statistical significance. All statistical analyses were performed using Stata/MP16 (StataCorp College Station, TX, USA). The study was approved by the Alfred Health Human Research Ethics Committee (HREC/16/Alfred/98).

Results

A total of 1,626 men who had definitive EBRT between 2015 and 2020 were included in the study (Fig. 1). Of these, 88 (5.4 %) had EBRT + BT (Table 1). There was no significant change in utilisation of EBRT + BT use over time – 6.2 % (27/437) in 2015–2016, 4.8 % (31/640) in 2017–2018, and 5.5 % (30/549) in 2019–2020 (P = 0.6). Higher proportion of younger men had EBRT-BT – 17 % (12/72) in men aged under 60 years, compared to 1.7 % (31/178) in men aged 80 years and above (P < 0.001). There were no statistically significant differences in EBRT + BT use by ISUP Grade Group, PSA level, clinical T categories and NCCN risk categories, as well as ADT use. There was a higher proportion of EBRT + BT use in men from the highest socioeconomic quintiles (36/360, 10 %) compared to those from the lowest socioeconomic quintiles (8/341, 2.3 %) (P < 0.001). There was also higher proportion of EBRT + BT use in men who lived in major city (77/963, 8.0 %) compared to regional or remote area (116/660, 1.7 %) (P < 0.001). Men treated in public institutions were also more likely to have EBRT + BT (74/1120, 6.6 %) compared to those treated in private institutions (14/506, 2.8 %) (P = 0.002). Men treated in metropolitan centres were also more likely to have EBRT + BT (84/1013, 8.3 %) compared to those treated in regional centres (4/613, 0.6 %) (P < 0.001).

In multivariable analyses, covariables that were independently associated with EBRT + BT use were age at treatment, socioeconomic status, and treatment centres and location (Table 2). For every 5 years increase in age, there is a relative 36 % (OR = 0.64; 95 %CI = 0.54–0.76; P < 0.001) reduced likelihood of having EBRT + BT. Men from the highest socioeconomic quintiles were more likely to have EBRT + BT compared to men from lowest socioeconomic quintiles (OR = 4.27; 95 % CI = 1.74–10.48; P = 0.002). Compared to men who had treatment in public institutions, those treated in private institutions were less likely to have EBRT + BT (OR = 0.24; 95 %CI = 0.12–0.48; P < 0.001).

There were 1555 (96 %) men who completed the EPIC-26 questionnaire (Fig. 1). The EPIC-26 questionnaires were completed at a median of 13.5 months post treatment (IQR: 13.0–13.9 months) and this
did not vary between the two groups (P = 0.8). Overall, there were high EPIC-26 urinary and bowel functions domain score in all men included in the study (Table 3). There were no statistically or clinically significant differences in EPIC-26 score for urinary, bowel and sexual function domain between men who had EBRT vs EBRT + BT - the adjusted mean differences in urinary incontinence, urinary obstructive, sexual, and bowel function domain scores between EBRT and EBRT + BT were: 1.28 (95 %CI = −3.23 to 5.79), −2.87 (95 %CI = −6.46 to 0.73), 0.49 (95 % CI = −4.78 to 5.76), and 2.89 (95 %CI = −0.83 to 6.61) respectively, and none reach the MCID. There was better hormonal function domain score in men who had EBRT + BT compared to men who had EBRT alone, with adjusted mean differences of 4.45 (95 %CI = 0.11−8.79). However, the lower margin of the 95 %CI is less than MCID of 4 points for hormonal function domain, hence there is uncertainty whether the difference is clinically significant.

**Discussion**

In this contemporary Australian population-based study, we reported persistent low utilisation of BT-boost in men who had EBRT for localized prostate cancer, compared to earlier study period [12]. This is the first time that PRO between men who had EBRT vs EBRT + BT is reported at a population-based level in Australia.

The decline and under-utilisation of BT in prostate cancer is well-recognized and have been reported in multiple population-based studies using the US National Cancer Database (NCDB) [6–10] and Surveillance, Epidemiology and End Results (SEER) [11] database. Previous Australian population-based study between 2010 and 2015 reported only 7 % of men who had EBRT for prostate cancer had BT-boost [12], and in the current study BT-boost utilisation remains low at 5.4 %. This is similar to a UK linkage study between the UK Cancer Registry, National Radiotherapy Dataset (RTDS), and Hospital Episodes Statistics (HES), which showed that of the 54,642 men who had EBRT for prostate cancer between 2010 and 2016, 3,095 (6 %) had BT-boost [27]. This contrasts with the findings in a Canadian study, which reported increasing BT utilisation in Ontario between 2006 and 2017, and this is largely driven by BT-boost in men who had EBRT, instead of BT monotherapy [31]. Among all men who had EBRT for prostate cancer, the proportion who had EBRT + BT-boost increased from 4 % in 2007 to 21 % in 2017 [31]. The observed differences in the trend of BT utilisation in Canada and the other studies are likely multifactorial, including differences in patient population, provider factors, as well as healthcare funding model [31]. Nonetheless, we believe that the low utilisation of BT boost is unlikely to change within the current Australian healthcare setting, unless there is convincing high-level evidence showing improved oncological outcomes of BT-boost beyond biochemical survival benefits compared to other novel techniques in the era of dose-escalated radiation therapy, such as stereotactic body radiation therapy, and that more radiation oncologists are well-trained in BT [16].

We observed variations in the utilisation of BT-boost. Unsurprisingly, younger men were more likely to have BT-boost, and this could be due to combination of reasons. Elderly patients are more likely to have multiple medical comorbidities and deemed medically unfit for operative procedures e.g., on long-term anticoagulation that may be unsafe to be discontinued for BT procedure. However, data on comorbidities was not consistently collected in PCOR-Vic to be included in our analyses. Also, local failure following radiation therapy has been shown to be prognostic for long-term risk of distant metastases and overall survival [32], and younger men may have less competing risk of death in the longer term and will derive greater benefit from the improved local control from BT boost [2–4]. We did not observe differences in utilisation of BT-boost by ADT use. Some of the earlier studies have suggested that clinicians may omit ADT in the setting of dose escalation with BT-boost [33]. However, individual patient-data meta-analyses from multiple randomised trials have shown that dose escalation alone in the absence of ADT did not improve oncological outcomes [34].

We reported higher utilisation of BT-boost in men from higher socioeconomic status in Australia. This pattern of higher BT utilisation in patients with higher income or socioeconomic group have been previously reported in the US [7,11]. This may reflect patients’ access to medical information, and these patients (from higher socioeconomic group) may have sought second opinions and treatment in centres that offer BT services. At the same time, we observed lower utilisation of BT-boost in patient treated in private centres, and this is likely reflective of the general decline in the interest in BT services in private centres. It is also important to note that while evidence from the most recent ASCENDE-BT trial used LDR-BT as BT-boost, LDR-BT is only funded as monotherapy for low to intermediate risk prostate cancer in the current Australian Medicare Benefits Schedule (MBS), and hence, all BT-boost delivered in combination with EBRT in Australia were HDR-BT. HDR-BT service provision is generally centralised given the high resource need. Apart from lower reimbursement for prostate BT, the disadvantageous manner in which capital costs for BT technology is supported in both public and private facilities, compared to capital support for new or replacement of LINACs, have largely limited the options of BT-boost for prostate cancer to men treated in two main public metropolitan radiation oncology facilities in Victoria with HDR-BT services.

A major strength of the current study is the use of validated PRO tools, consistent with recommendation by international consortium group [35], to capture toxicity outcomes at a population-based level,
Table 1
Patient, tumor, and treatment characteristics of the study cohort.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Overall N = 1538</th>
<th>EBRT alone N = 888 (56.4 %)</th>
<th>EBRT + BT N = 1550 (45.6 %)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year of treatment</td>
<td></td>
<td></td>
<td></td>
<td>0.6</td>
</tr>
<tr>
<td>2015–2016</td>
<td>437 (26.9 %)</td>
<td>410 (93.8 %)</td>
<td>27 (6.2 %)</td>
<td></td>
</tr>
<tr>
<td>2017–2018</td>
<td>640 (39.4 %)</td>
<td>609 (95.2 %)</td>
<td>31 (4.8 %)</td>
<td></td>
</tr>
<tr>
<td>2019–2020</td>
<td>549 (33.8 %)</td>
<td>519 (94.5 %)</td>
<td>30 (5.5 %)</td>
<td></td>
</tr>
<tr>
<td>Age at treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>72.8 (6.5)</td>
<td>73.0 (6.4)</td>
<td>69.4 (6.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&lt; 60</td>
<td>72 (4.4 %)</td>
<td>60 (83.3 %)</td>
<td>12 (16.7 %)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>60–69</td>
<td>417 (25.7 %)</td>
<td>387 (92.8 %)</td>
<td>30 (7.2 %)</td>
<td></td>
</tr>
<tr>
<td>70–79</td>
<td>959 (59.0 %)</td>
<td>916 (95.5 %)</td>
<td>43 (4.5 %)</td>
<td></td>
</tr>
<tr>
<td>&gt; 80</td>
<td>178 (11.0 %)</td>
<td>175 (98.3 %)</td>
<td>3 (1.7 %)</td>
<td></td>
</tr>
<tr>
<td>PSA at diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>9.5</td>
<td>9.5</td>
<td>9.7</td>
<td>0.5</td>
</tr>
<tr>
<td>&lt; 10 ng/mL</td>
<td>817 (50.3 %)</td>
<td>775 (94.9 %)</td>
<td>43 (5.1 %)</td>
<td>0.5</td>
</tr>
<tr>
<td>10–20 ng/mL</td>
<td>486 (29.9 %)</td>
<td>456 (93.4 %)</td>
<td>34 (6.6 %)</td>
<td></td>
</tr>
<tr>
<td>&gt; 20 ng/mL</td>
<td>211 (13.0 %)</td>
<td>203 (95.7 %)</td>
<td>9 (4.3 %)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>112 (6.9 %)</td>
<td>110 (95.5 %)</td>
<td>5 (4.5 %)</td>
<td>0.3</td>
</tr>
<tr>
<td>ISUP Grade Group</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1</td>
<td>65 (4.0 %)</td>
<td>64 (98.5 %)</td>
<td>1 (1.5 %)</td>
<td></td>
</tr>
<tr>
<td>Group 2</td>
<td>509 (31.3 %)</td>
<td>485 (95.3 %)</td>
<td>25 (4.7 %)</td>
<td></td>
</tr>
<tr>
<td>Group 3</td>
<td>415 (25.5 %)</td>
<td>393 (94.7 %)</td>
<td>22 (5.3 %)</td>
<td></td>
</tr>
<tr>
<td>Group 4</td>
<td>259 (15.9 %)</td>
<td>238 (91.9 %)</td>
<td>21 (8.1 %)</td>
<td></td>
</tr>
<tr>
<td>Group 5</td>
<td>316 (19.4 %)</td>
<td>299 (94.6 %)</td>
<td>17 (5.4 %)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>62 (3.8 %)</td>
<td>59 (95.2 %)</td>
<td>3 (4.8 %)</td>
<td>0.07</td>
</tr>
<tr>
<td>Clinical T categories</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>496 (30.5 %)</td>
<td>462 (93.2 %)</td>
<td>34 (6.9 %)</td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>644 (39.6 %)</td>
<td>605 (93.9 %)</td>
<td>41 (6.1 %)</td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>134 (8.2 %)</td>
<td>128 (95.5 %)</td>
<td>6 (4.5 %)</td>
<td></td>
</tr>
<tr>
<td>T4</td>
<td>15 (0.9 %)</td>
<td>15 (100 %)</td>
<td>0 (0 %)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>337 (20.7 %)</td>
<td>328 (97.3 %)</td>
<td>9 (2.7 %)</td>
<td></td>
</tr>
<tr>
<td>NCCN risk categories</td>
<td></td>
<td></td>
<td></td>
<td>0.6</td>
</tr>
<tr>
<td>Low/intermediate</td>
<td>30 (1.8 %)</td>
<td>29 (96.7 %)</td>
<td>1 (3.3 %)</td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>662 (40.7 %)</td>
<td>627 (94.7 %)</td>
<td>35 (5.3 %)</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>744 (45.8 %)</td>
<td>699 (94.0 %)</td>
<td>45 (6.1 %)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>190 (11.7 %)</td>
<td>183 (96.3 %)</td>
<td>7 (3.7 %)</td>
<td></td>
</tr>
<tr>
<td>Androgen deprivation therapy use</td>
<td></td>
<td></td>
<td></td>
<td>0.1</td>
</tr>
<tr>
<td>No</td>
<td>515 (31.7 %)</td>
<td>494 (95.9 %)</td>
<td>21 (4.1 %)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1111 (68.3 %)</td>
<td>1044 (94.0 %)</td>
<td>67 (6.0 %)</td>
<td></td>
</tr>
<tr>
<td>Socioeconomic status</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Quintile 1 (lowest)</td>
<td>341 (21.0 %)</td>
<td>333 (97.7 %)</td>
<td>8 (2.3 %)</td>
<td></td>
</tr>
<tr>
<td>Quintile 2</td>
<td>313 (19.3 %)</td>
<td>307 (98.1 %)</td>
<td>6 (1.9 %)</td>
<td></td>
</tr>
<tr>
<td>Quintile 3</td>
<td>275 (16.9 %)</td>
<td>259 (94.2 %)</td>
<td>16 (5.8 %)</td>
<td></td>
</tr>
<tr>
<td>Quintile 4</td>
<td>334 (20.5 %)</td>
<td>312 (93.4 %)</td>
<td>22 (6.6 %)</td>
<td></td>
</tr>
<tr>
<td>Quintile 5 (highest)</td>
<td>360 (22.1 %)</td>
<td>324 (90 %)</td>
<td>36 (10 %)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>3 (0.2 %)</td>
<td>3 (100 %)</td>
<td>0 (0 %)</td>
<td></td>
</tr>
</tbody>
</table>

EBRT = external beam radiation therapy; BT = brachytherapy.

Table 2
Covariates associated with use of brachytherapy boost with external beam radiation therapy.

<table>
<thead>
<tr>
<th>Covariate</th>
<th>OR (95 %CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year of treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2015–2016</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>2017–2018</td>
<td>0.82 (0.46–1.44)</td>
<td>0.5</td>
</tr>
<tr>
<td>2019–2020</td>
<td>0.94 (0.51–1.70)</td>
<td>0.8</td>
</tr>
<tr>
<td>Age at treatment (for every 5 years increase)</td>
<td>0.64 (0.54–0.76)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NCCN risk categories</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low/intermediate</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>1.18 (0.70–2.00)</td>
<td>0.5</td>
</tr>
<tr>
<td>Androgen deprivation therapy use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.40 (0.75–2.59)</td>
<td>0.3</td>
</tr>
<tr>
<td>Socioeconomic status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quintile 1 (lowest)</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Quintile 2</td>
<td>1.29 (0.42–4.00)</td>
<td>0.7</td>
</tr>
<tr>
<td>Quintile 3</td>
<td>2.57 (0.99–6.70)</td>
<td>0.05</td>
</tr>
<tr>
<td>Quintile 4</td>
<td>3.07 (1.22–7.72)</td>
<td>0.02</td>
</tr>
<tr>
<td>Quintile 5 (highest)</td>
<td>4.27 (1.74–10.48)</td>
<td>0.002</td>
</tr>
<tr>
<td>Area of residence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major city</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Regional/remote</td>
<td>0.25 (0.12–0.52)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

EBRT = external beam radiation therapy; BT = brachytherapy.

The use of PRO is increasingly being recognized, and is commonly incorporated in clinical trials these days. We did not observe statistically or clinically significant differences in PRO for urinary, bowel and sexual function between men who had EBRT vs EBRT + BT at a population-based level in Australia (Table 3). However, we have to acknowledge the limitation of the use of convenience sample of real-world data, whereby there is disproportionately small number of patients who had EBRT + BT in our cohort, with resultant large range in confidence interval and uncertainty in the observed (lack of) differences in PRO. Nonetheless, we did observe statistically significant difference in hormonal domain score between the two groups. This is reflective of the impact of ADT rather than that of BT-boost. While there were no differences in ADT use between the two groups (Table 1), the difference in the hormonal domain score is most likely reflective of the duration of ADT use in the two groups (which were not captured in PCOR-Vic) in relation to the timing of completion which allows us to continuously monitor and benchmark radiation therapy practice across different centres. Given that clinicians often under-estimate patients’ symptoms [36], the use of PRO is increasingly being recognized, and is commonly incorporated in clinical trials these days. We did not observe statistically or clinically significant differences in PRO for urinary, bowel and sexual function between men who had EBRT vs EBRT + BT at a population-based level in Australia (Table 3). However, we have to acknowledge the limitation of the use of convenience sample of real-world data, whereby there is disproportionately small number of patients who had EBRT + BT in our cohort, with resultant large range in confidence interval and uncertainty in the observed (lack of) differences in PRO. Nonetheless, we did observe statistically significant difference in hormonal domain score between the two groups. This is reflective of the impact of ADT rather than that of BT-boost. While there were no differences in ADT use between the two groups (Table 1), the difference in the hormonal domain score is most likely reflective of the duration of ADT use in the two groups (which were not captured in PCOR-Vic) in relation to the timing of completion.
Clinical and Translational Radiation Oncology 37 (2022) 19–24

of the EPIC-26 questionnaire.

The only other population-based study that had reported on PRO, using the EPIC-26 questionnaire, between men who had EBRT and EBRT + BT was from the UK National Prostate Cancer Audit (NPCA) [26]. In that study, Parry et al reported worse urinary obstructive/obstructive domain score with EBRT + BT compared to EBRT alone (mean adjusted difference: −6.1, 95% CI: −8.8 to −3.4); however, it is uncertain as to whether it is clinically significant [26]. When comparing our findings with that from the UK NPCA, we observed consistently higher EPIC domain scores for men who had EBRT with or without BT across all functional domains, despite the EPIC questionnaire being completed at a similar period of approximately 12 months post-treatment (Table 4). This is an important finding for future international benchmarking effort, as it appears to suggest that at a population-based level, men treated with EBRT + BT in Australia had better PRO compared to men treated in the UK. However, a common limitation in both NPCA and PCOR-Vic, is the lack of information on pre-treatment PRO. Earlier studies have shown that different level of pre-treatment function produced distinct treatment-related changes from baseline [37]. It remains unknown if men in the UK had worse pre-treatment function, or if they had bigger decline in functional outcomes following treatment, compared to men in Australia.

Apart from the lack of pre-treatment PRO, there are several other limitations in the current study, which are inherent limitations within the PCOR-Vic dataset. Given that some of the late treatment-related toxicities may be delayed for years, it will be important to capture and compare the late PRO between EBRT and EBRT + BT. However, current funding within PCOR-Vic has limited PRO collection up to 12 months post-treatment, and future funding is required to allow assessment of longer-term follow-up for men enrolled in PCOR-Vic. There are varying dose-fractionation schedules used for EBRT component which may confound the PRO; however, previous Australian population-based study has shown no clinically significant difference in PRO between men treated with conventional fractionated and hypofractionated EBRT [38].

Conclusion

In summary, the most contemporary Australian population-based data suggests that utilisation of BT-boost with EBRT for prostate cancer remains low compared to earlier studies. Within the limitation of the study, reassuringly, there is no evidence at a population-based level indicating clinically significant differences in PRO in men who had EBRT compared to EBRT + BT at 12 months post-treatment. However, longer-term follow-up is required. The current findings also need to be interpreted in the absence of baseline PRO, and future work is needed to enable collection of baseline PRO in men enrolled in PCOR-Vic.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

The Prostate Cancer Outcomes Registry Victoria (PCOR-Vic) is funded by Movember Foundation.

Data sharing

Research data is stored in institutional repository and will be shared upon reasonable request to the corresponding author.

References


