**Table 1. Patient characteristics and clinical outcomes[a]**

| Study | Study type | Treatment (dose) | Risk category[b] (n) | Mean or median age (yr) | Survival Outcome | | | bRFS Outcome | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Time (yr) | Survival | *p*-value | Time (yr) | bRFS | *p* value |
| **Research Question 1. Comparisons with PB alone** | | | | | | | | | | |
| Giberti 2009[c 37] | RCT | 1. PB[d] (>140 Gy I-125)<br>2. RP[e] | Low (100)<br>Low (100) | 66<br>65 | NA | | | 5 | 92%<br>91% | NS |
| D'Amico 1998[c 31] | Retrosp. | 1. PB[f] (115 Gy Pd-103)<br>2. EBRT[f] (66-70 Gy)<br>3. RP[f] | Low (32)<br>Low (225)<br>Low (402) | NA | NA | | | 5 | NA | 1. vs. 2.: $p>0.25$;<br>1. vs. 3.: $p>0.25$ |
| | | 1. PB[f] (115 Gy Pd-103) + neo-HT<br>2. EBRT[f] (66-70 Gy) | Low (91)<br>Low (225) | NA | NA | | | 5 | NA | $p>0.25$ |
| | | | Int[g] (38)<br>Int[g] (232) | NA | NA | | | 5 | NA | $p=0.009$[h,i] |
| | | 1. PB[f] (115 Gy Pd-103) + neo-HT<br>2. RP[f] | Low (91)<br>Low (402) | NA | NA | | | 5 | NA | $p>0.25$ |
| | | | Int[g] (38)<br>Int[g] (247) | NA | NA | | | 5 | NA | $p=0.18$[i] |
| Tward 2006[j,k 65] | Retrosp. | Men < 60 y | | | | PCSM OS | | | | |
| | | 1. PB | Low/Int (1,233) | 56 | 10 | 0.5% 92.1% | NS | NA | | |
| | | 2. RP | Low/Int (11,566) | 55 | | 1.3% 92.2% | | | | |
| | | Men > 60 y | | | | | | | | |
| | | 1. PB | Low/Int (5,404) | 69 | | 5.3% 62.9% | | | | |
| | | 2. RP | Low/Int (23,192) | 66 | | 3.8% 72.6% | | | | |
| Burdick 2009[l,k 26] | Retrosp. | 1. PB[d] (144 Gy for I-125)<br>2. EBRT[d] (minimum of 70 Gy)<br>3. RP[m] | Low/Int/≤20% high (127)<br>Low/Int/≤20% high (268)<br>Low/Int/≤20% high (310) | 66 | NA | | | 5 | 1. vs. 2.: HR=1.04<br>1. vs. 3.: HR=0.44 | NS<br>$p=0.004$[n] |
| Vassil 2010[l,k 66] | Retrosp. | 1. PB[d] (144 Gy I-125)<br>2. EBRT[d] (70-80 Gy)<br>3. LRP[o]<br>4. RRP[o] | Int (256)<br>Int (305)<br>Int (64)<br>Int (354) | 69<br>68<br>63<br>62 | NA | | | 5 | 90%<br>86%<br>60%<br>80% | 1. vs. 2.: $p=0.969$;<br>1. vs. 3.: $p<0.001$[n];<br>1. vs. 4.: $p=0.003$[n] |

N: sample size; y: year; bRFS: biochemical relapse-free survival; PB: low-dose rate brachytherapy; RCT: randomized controlled trial; Gy: gray; I-125: iodine-125; RP: radical prostatectomy; NA: not available; NS: not statistically significant; Retrosp: retrospective study; Pd-103: palladium-103; EBRT: external beam radiation therapy; neo-HT: neo-adjuvant hormonal therapy; Int: intermediate; PCSM: prostate cancer-specific mortality; OS: overall survival; HR: hazard ratio; LRP: laparoscopic RP; RRP: retropubic RP; Prosp: prospective study; Cs-131: cesium-131; 3D-CRT: 3-D conformed radiation therapy; IMRT: intensity-modulated radiotherapy.

aStudies are in italics if they were non-RCT and did not clarify that there was no significant difference in the baseline patient characteristics among treatment groups or they did not use multivariate analysis to adjust for confounding factors when reporting outcomes. Thus, italic entries are more subject to bias in their reported outcomes. bLow-risk patients were defined as having prostate-specific antigen (PSA) <10 ng/mL and clinical stage T1c to T2a and Gleason score <7, intermediate-risk patients were defined as having PSA <20 ng/mL or clinical stage T2b-T2c or Gleason score =7 and are not otherwise low-risk patients, high-risk patients were defined as having PSA ≥20 ng/mL or clinical stage >T2c or Gleason score >7 in tumour. cThe baseline clinical characteristics were not significantly different among the intervention groups. dThe biochemical failure followed the Radiation Therapy Oncology Group (RTOG) of the American Society of Therapeutic Radiation and Oncology (ASTRO) Phoenix consensus that PSA should be higher than nadir plus 2 ng/mL. eThe biochemical failure was defined as two consecutive PSA values ≥0.2 ng/mL. fThe definition of failed PSA followed the ASTRO 1996 consensus statement that patients had three consecutive rising PSA values each obtained at least three months apart. gIntermediate-risk patients were defined as having PSA <20 ng/mL or ≥10 ng/mL, clinical stage T2b, or Gleason score = 7; high-risk patients were defined as having PSA ≥ 20 ng/ml or clinical stage ≥ T2c or Gleason score > 7 in tumour. hSignificance favoured ERBT. iThe original author stated that the study was not adequately powered to detect this difference. jThere was no statistical comparison for patient characteristics at the baseline between intervention groups. kMultivariate analysis was used to adjust baseline confounders. lThe baseline clinical characteristics were significantly different among the intervention groups. mIn the RP group, a PSA level >0.3 ng/mL was considered a failure. nSignificance favoured PB. oIn the RP group, a PSA level ≥0.4 ng/mL was considered a failure. pIn the RP group, a PSA level >0.2 ng/mL was considered a failure. qThe baseline characteristics were not significantly different among the intervention groups except that patients in RP group with nerve-sparing procedure were younger. rIn the RP group, a PSA level >0.1 ng/mL was considered a failure. sSignificance favoured RP. tIn the PB group, a PSA level >1.5 ng/mL with a positive biopsy; or a PSA level >1.5 ng/mL that was higher than the previous one was considered a failure. uThe biochemical failure was defined as a PSA >0.5 ng/mL after nadir.

**Table 1. Patient characteristics and clinical outcomes[a] (cont'd)**

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|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Time (yr) | Survival | *p*-value | Time (yr) | bRFS | *p* value |
| **Research Question 1. Comparisons with PB alone** | | | | | | | | | | |
| *D'Amico 2003*[i 30] | Retrosp. | 1. PB[d]<br>2. RP[p] | Low/Int (227)<br>Low/Int (406) | 62<br>60 | NA | | | 5 | 95%<br>93% | NS |
| *Borchers 2004*[q 25] | Prosp. | 1. PB[d]<br>2. RP[r] | Low (52)<br>Low (80) | 67<br>62 | NA | | | 2.3 | 85%<br>96% | *p*=0.04[s] |
| *Kupelian 2004*[l 43] | Retrosp. | 1. PB[f] (144 Gy I-125/136 Gy Pd-103)<br>2. EBRT[f] (72-83 Gy)<br>3. EBRT+PB[f] (41.4 Gy EBRT+108 Gy I-125 or 45 Gy EBRT+102 Gy Pd-103)<br>4. RP[p] | Low (unclear) | 70<br>68<br>69<br>63 | NA | | | 7 | NA | *p*=0.18 |
| *Klein 2009*[j 42] | Retrosp. | 1. PB[d] (144 Gy I-125)<br>2. 3D-CRT or EBRTd (median 81 Gy)<br>3. RP[m] | Intg (204)<br>Intg (321)<br>Intg (336) | NA | 8 | OS:94%<br>82%<br>88% | *p*=0.046 | 8 | 82%<br>75%<br>63% | *p*=0.052 |
| *Arvold 2011*[l,k 22] | Prosp. | 1. PB (144 Gy I-125;108 Gy Pd-103 or Cs-131)<br>2. RP (some receiving adjuvant EBRT) | Low (3,851)<br>Low (1,909) | 69<br>61 | 4.2 | PCSM: HR=1.62 | *p*=0.35 | NA | | |
| | | | Int (2,051)<br>Int (1,028) | 71<br>63 | 4.8 | PCSM: HR=2.30 | *p*=0.07 | NA | | |
| *Zelefsky 2011*[l 74] | Retrosp. | 1. PB[d] (144 Gy I-125)<br>2. EBRT[d] (81 Gy) | Low (448)<br>Low (281) | 62% of pts ≥65 | NA | | | 7 | 95%<br>89% | *p*=0.004[n] |

N: sample size; y: year; bRFS: biochemical relapse-free survival; PB: low-dose rate brachytherapy; RCT: randomized controlled trial; Gy: gray; I-125: iodine-125; RP: radical prostatectomy; NA: not available; NS: not statistically significant; Retrosp: retrospective study; Pd-103: palladium-103; EBRT: external beam radiation therapy; neo-HT: neo-adjuvant hormonal therapy; Int: intermediate; PCSM: prostate cancer-specific mortality; OS: overall survival; HR: hazard ratio; LRP: laparoscopic RP; RRP: retropubic RP; Prosp: prospective study; Cs-131: cesium-131; 3D-CRT: 3-D conformed radiation therapy; IMRT: intensity-modulated radiotherapy.

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|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Time (yr) | Survival | *p*-value | Time (yr) | bRFS | *p* value |
| **Studies with unclear proportion of high-risk patients** | | | | | | | | | | |
| *Wong 2009*[j,k 72] | Retrosp. | 1. PB[d] (144 Gy I-125 or 120 Gy Pd-103)<br>2. 3D-CRT[d] (66-71 Gy)<br>3. IMRT[d] (75.6-77.4 Gy)<br>4. 3D-CRT+PB[d] (45 Gy 3D-CRT + 110 Gy I-125 or 90 Gy Pd-103) | Low/Int/high (225)<br>Low/Int/high (270)<br>Low/Int/high (314)<br>Low/Int/high (44) | NA | NA | | | 5 | 94%<br>74%<br>87%<br>94% | *p*<0.001 |
| *Sharkey 2002*[j 56] | Retrosp. | 1. PB[t] (Pd-103)<br>2. RP | Low/Int/high: (869)<br>Low/Int/high: (208) | 72<br>64 | NA | | | 7 | 76%<br>74% | NS |
| **Research Question 2. Comparisons with EBRT+PB in combination** | | | | | | | | | | |
| Wallner 2005[c 69] | RCT | 1. EBRT (44 Gy) + PB[u] (90 Gy Pd-103)<br>2. EBRT (20 Gy) +PB[u] (115 Gy Pd-103) | Int/≤20% high (80)<br>Int/≤20% high (85) | 67<br>67 | NA | | | 3 | 88%<br>83% | NS |
| **Studies with unclear proportion of high-risk patients** | | | | | | | | | | |
| *Stock 2009*[j 63] | Retrosp. | 1. PB (120 Gy I-125 or 100 Gy Pd-103) + EBRT (median 45 Gy)<br>2. PB (160 Gy I-125 or 124 Gy Pd-103) | Low/Int/high (224)<br>Low/Int/high (518) | NA | NA | | | 10 | bRFS[f] 100%<br>95%<br>bRFS[d] 100%<br>93% | P[f]=0.5;<br>P[d]=0.7 |
| **Research Question 3. Comparison of I-125 and Pd-103** | | | | | | | | | | |
| Merrick 2007[c 47] | RCT | 1. I-125[u] (144 Gy)<br>2. Pd-103[u] (125 Gy) | Low (127)<br>Low (136) | 65<br>66 | NA | | | 6 | 96.8%<br>99.2% | NS |

N: sample size; y: year; bRFS: biochemical relapse-free survival; PB: low-dose rate brachytherapy; RCT: randomized controlled trial; Gy: gray; I-125: iodine-125; RP: radical prostatectomy; NA: not available; NS: not statistically significant; Retrosp: retrospective study; Pd-103: palladium-103; EBRT: external beam radiation therapy; neo-HT: neo-adjuvant hormonal therapy; Int: intermediate; PCSM: prostate cancer-specific mortality; OS: overall survival; HR: hazard ratio; LRP: laparoscopic RP; RRP: retropubic RP; Prosp: prospective study; Cs-131: cesium-131; 3D-CRT: 3-D conformed radiation therapy; IMRT: intensity-modulated radiotherapy.

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**Table 2. More than or equal to grade 2 toxicity**

| Study | Study type | Treatment (dose) | Risk patients[a] (n) | Mean or median age (y) | F-up time (y) | Second primary cancer | GU toxicity | Impotence | GI toxicity |
|---|---|---|---|---|---|---|---|---|---|
| **Research Question 1. Comparisons with PB** | | | | | | | | | |
| Abdel-Wahab 2008[b,c 21] | Retrosp. | 1. PB<br>2. EBRT | Low/Int/≤20% high (10,214)<br>Low/Int/≤20% high (48,225) | 67<br>71 | 2.8-3.3<br>4.2-5.0 | 4.7% vs. 10.3%, p<0.001[d] | NA | NA | NA |
| Zelefsky 2011[e,f 74] | Retrosp. | 1. PB (144 Gy I-125)<br>2. EBRT (81 Gy) | Low (448)<br>Low (281) | 62% of pts ≥65 | 6.4<br>6.4 | NA | Late grade 2: 15.6% vs. 4.3%, p<0.001[g]; Late grade 3: 2.2% vs. 1.4%, NS | Developed post-treatment impotence: 35% vs. 44%, *p*=0.04d | Late grade 2: 5.1% vs. 1.4%, *p*=0.018[g]; Late grade 3: 1.1% vs. 0.0%, NS |
| **Research Question 2. Comparisons with LDR-BT+EBRT** | | | | | | | | | |
| Gelblum 2000[i,j 35] | Retrosp. | 1. EBRT (41.4-45 Gy)+PB (100 Gy I-125/90 Gy Pd-103)<br>2. PB (144 Gy I-125/120 Gy Pd-103) | Low/Int/≤20% high (140)<br>Low/Int/≤20% high (685) | 67<br>67 | 4<br>4 | NA | NA | NA | Grade 2 at 8 months: 7.1% vs. 6.5%, NS; Grade 3 at 12 months: 0.7% vs. 0.4%, NS |
| **Unclear proportion of high-risk patients** | | | | | | | | | |
| Wong 2009[h,i 72] | Retrosp. | 1. PB (144 Gy I-125/120 Gy Pd-103)<br>2. 3D-CRT (66-71 Gy)<br>3. IMRT (75.6-77.4 Gy)<br>4. 3D-CRT+PB (45 Gy 3D-CRT+110 Gy I-125/90 Gy Pd-103) | 225<br>270<br>314<br>44 | NA | 4.1<br>5.2<br>4.7<br>5.3 | NA | 1). Acute grade 2: 68% vs. 39% vs. 49% vs. 73%, Acute grade 3: 6% vs. 1% vs. 3% vs. 2%. *p*<0.001[g]<br>2). Late grade 2: 45% vs. 16% vs. 27% vs. 52%, Late grade 3: 18% vs. 5% vs. 5% vs. 18%. *p*<0.001[g] | NA | 1). Acute grade 2: 8% vs. 54% vs. 45% vs. 11%, Acute grade 3: 0% vs. 0% vs. 1% vs. 0%. *p*<0.001[d]<br>2). Late grade 2: 12% vs. 15% vs. 14% vs. 23%, Late grade 3: 1% vs. 2% vs. 1% vs. 5%. *p*<0.001[d] |

N: sample size; y: year; F-up: follow-up; GU: genitourinary; GI: gastrointestinal; PB: low-dose rate brachytherapy; Gy: gray; I-125: iodine-125; pts: patients; NA: not available; Retrosp: retrospective study; Pd-103: palladium-103; EBRT: external beam radiation therapy; Int: intermediate; 3D-CRT: 3-D conformed radiation therapy; IMRT: intensity-modulated radiotherapy.

aLow-risk patients were defined as having prostate-specific antigen (PSA) <10 ng/mL and clinical stage T1c to T2a and Gleason score <7, intermediate-risk patients were defined as having PSA < 20 ng/ml or clinical stage T2b to T2c or Gleason score = 7 and are not otherwise low-risk patients, high-risk patients were defined as having PSA ≥20 ng/mL or clinical stage >T2c or Gleason score >7 in tumour. bPatients with grade I had Gleason scores 2-4 and patients with grade II had Gleason scores 5-7 and patients with grade III had Gleason scores 8-10 before January 1st, 2003, but after 2003, patients with Gleason score 7 moved to grade III. cThere was no statistical comparison for patient characteristics at the baseline between intervention groups. However, the EBRT group had more patients ≥65 years old (82% vs. 63%) and more high-risk patients (19.6% vs. 5.4%) than those in the PB group. dSignificance favoured PB. eToxicity was measured by National Cancer Institute Common Toxicity Criteria for Adverse Events, version 3.0 toxicity scale. fAt the baseline, patients were older and had earlier T stages in the PB group than those in the EBRT group (p < 0.01). gSignificance favoured 3D-CRT or IMRT. hThere was no statistical comparison for patient characteristics at the baseline between intervention groups. However, the lowest proportion of high-risk patients was in the PB group. iToxicity was measured by a modified Radiation Therapy Oncology Group scale. jThere was no statistical comparison for patient characteristics at the baseline between intervention groups.

**Table 3. Key evidence for patient-reported outcomes[a]**

| Treatment[b] | PRO/QOL | Favouring PB | No Significant Difference | Favouring Comparator |
|---|---|---|---|---|
| **Research Question 1. Comparisons with PB** | | | | |
| PB vs. EBRT | **Urinary incontinence** | | NS at 2-3 y[33,51] | |
| | Urinary irritation | | NS at 2-3 y[33,51] | |
| | Sexual function | Favoured PB at 2-3 y[33,51] | | |
| | Rectal morbidity | Favoured PB at 2-3 y[33,51] | | |
| | Overall QOL | | NS at 3 y[51] | |
| PB vs. RP | Urinary incontinence | Favoured PB at 6 mo[37]<br>Favoured PB at 2-3 y[27,38,51] | NS at 12 mo and 5 y[37] | |
| | Urinary irritation | | NS at 5 y[37] | Favoured RP at 6 and 12 mo[37]<br>Favoured RP at 2-3 y[27,33,38,51] |
| | Sexual function | Favoured PB at 6 and 12 mo[37]<br>Favoured PB at 12 mo[25]<br>Favoured PB at 18 mo to 3 y[27,33,38,51] | NS at 5 y[37] | |
| | Rectal morbidity | | NS at 12 mo and 5 y[37]<br>NS at 2-3 y [33,38,51] | Favoured RP at 6 mo[37]<br>Favoured RP at 2 y[27] |
| | Overall QOL | | NS, both PB and RP decreased by 1 y; returned to baseline level at 5 y[37]<br>NS at 12 mo[25]<br>NS at 2-3 y[38,51] | Favoured RP at 2 y[27] |
| **Research Question 2. Comparisons with PB+EBRT** | | | | |
| EBRT + PB vs. PB | Urinary function and bother | Favoured PB at 21 mo[73] | | |
| | Sexual function and bother | | NS at 21 mo[73] | |
| | Rectal function and bother | | NS at 21-24 mo[58,73] | |
| | Overall QOL | | NS at 21 mo73 | |
| **Research Question 3. Comparisons of I-125 with Pd-103** | | | | |
| I-125 vs. Pd-103 | AUA score | Favoured I-125 at 1 mo[39] | NS at 12 and 24 mo[39] | Favoured Pd-103 at 6 mo[39] |
| | Rectal morbidity | Favoured I-125 at 1 mo[36] | NS at 3,6, and 12 mo[36] | |

PRO: patient reported outcomes; QOL: quality of life; PB: low-dose rate brachytherapy; EBRT: external beam radiation therapy; NS: not statistically significant; y: years; RP: radical prostatectomy; mo: months; I-125: iodine-125; Pd-103: palladium-103; AUA: American Urological Association Symptom Index.

aOnly randomized controlled trials and the following studies that included clear low-risk, intermediate-risk, or ≤20% high-risk patients are shown in the table: patient QOL among intervention groups was not statistically different at the baseline, the QOL changes from the baseline and the end of the study were compared, or studies adjusted the potential confounding factors. bSome patients may have neo-adjuvant hormonal therapy in any treatment group.