<table>
<tr><th>Study, country</th><th>Study type, study period</th><th>Number of patients</th><th>Patient characteristics</th><th>Intervention</th><th>Comparison</th><th>Length of follow-up</th><th>Outcome measures and effect size</th><th>Source of funding</th><th>Additional comments</th></tr>
<tr>
<td>Duchesne 2000

UK</td>
<td>Randomised trial

1992-1997</td>
<td>500 patients (460 included in symptom improvement analysis) MIBC causing local symptoms, life expectancy at least 3 months, no chemo. Either unfit for radical treatment because of age or general medical condition, or tumour stage too advanced for radical treatment (T4b,N+,M1).</td>
<td>
<table>
<tr><th></th><th>35 Gy-10 N (%)</th><th>21 Gy-3 N (%)</th></tr>
<tr><td>Median age</td><td>79</td><td>80</td></tr>
<tr><td>Male</td><td>182 (73)</td><td>181 (72)</td></tr>
<tr><td>Female</td><td>66 (27)</td><td>71 (28)</td></tr>
<tr><td>PS 0</td><td>28 (11)</td><td>32 (13)</td></tr>
<tr><td>PS 1</td><td>116 (47)</td><td>122 (49)</td></tr>
<tr><td>PS 2</td><td>83 (34)</td><td>82 (33)</td></tr>
<tr><td>PS 3</td><td>19 (8)</td><td>14 (5)</td></tr>
<tr><td>Unfit for Rx</td><td>164 (66)</td><td>157 (62)</td></tr>
<tr><td>Too advanced</td><td>84 (34)</td><td>95 (38)</td></tr>
<tr><td>TCC</td><td>228 (93)</td><td>226 (90)</td></tr>
<tr><td>G1</td><td>3 (1)</td><td>5 (2)</td></tr>
<tr><td>G2</td><td>47 (19)</td><td>41 (16)</td></tr>
<tr><td>G3</td><td>190 (77)</td><td>195 (78)</td></tr>
<tr><td>Gx</td><td>6 (3)</td><td>10 (4)</td></tr>
<tr><td>N0</td><td>85 (34)</td><td>71 (28)</td></tr>
<tr><td>N+</td><td>29 (12)</td><td>53 (21)</td></tr>
<tr><td>Nx</td><td>133 (54)</td><td>128 (51)</td></tr>
<tr><td>M0</td><td>132 (54)</td><td>137 (54)</td></tr>
<tr><td>M1</td><td>13 (5)</td><td>27 (11)</td></tr>
<tr><td>Mx</td><td>102 (41)</td><td>88 (35)</td></tr>
<tr><td>Hem g/dl</td><td></td><td></td></tr>
<tr><td><10</td><td>36 (15)</td><td>30 (13)</td></tr>
<tr><td>≥10</td><td>203 (85)</td><td>210 (87)</td></tr>
<tr><td>SCr</td><td></td><td></td></tr>
<tr><td>Normal</td><td>121 (52)</td><td>115 (49)</td></tr>
<tr><td>elevated</td><td>111 (48)</td><td>121 (51)</td></tr>
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</td>
<td>21 Gy in 3 fractions on alternate weekdays over 1 week

RT planning and treatment at discretion of clinician although advised that megavoltage irradiation used and treatment volume should encompass the bladder and tumour and not whole pelvis. 2, 3, or 4 field techniques were permissible, preferably treating all fields for each fraction.</td>
<td>35 Gy in 10 fractions over 2 weeks</td>
<td>3-month assessment for symptomatic assessment. Median follow-up for OS not reported.</td>
<td>Symptom improvement: 120/225 (53%) 35-Gy and 115/232 (50%) 210Gy had noted overall bladder and bowel symptomatic improvement by end-of-treatment assessment. Absolute difference 3% (-6% to 12%).
No evidence of a difference between treatments for changes of symptoms from pre-treatment to 3-month assessment.
Haematuria alleviated in 88%, frequency in 82%, dysuria in 72% and nocturia in 64%.
95/133 (71%) 35-Gy and 89/139 (64%) 21-Gy achieved overall symptomatic improvement from pre-treatment to 3-month assessment Absolute difference 7% (-2% to 13%).
Quality of life (Rotterdam Symptom</td>
<td>MRC</td>
<td>Adequate randomisation, groups comparable at baseline, power calculations conducted, similar drop-out rate in both groups. Reasons for lack of data at 3-month assessment similar in both groups.</td>
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							Checklist): Most patients reported no overall change or an improvement. No difference in change of any symptom between 2 treatment arms. **Overall survival:** 402 (204/248 35Gy, 198/252 21-Gy) patients died (HR 0.99, 0.82-1.21). 3-mo survival 77% in both arms. Median survival=7.5mo		
Srinivasan (1994) UK	Observational study (appears retrospective) 1982-1989	41 patients T3-4, Grade 2-3 TCC treated by palliative radiotherapy	19 patients with reasonable PS (WHO grade ≤3) treated with conventional palliative treatment; 22 patients with poor performance status (WHO grade ≥4) accelerated radiotherapy. Mean age 78.4 years in 2-fraction group compared to 71.6 y in conventional group.	Conventional palliative treatment 4500cGy in 12 fractions over 26 days Both used supervoltage photons. From 1984 volume was localised with CT.	Accelerated radiotherapy 1700cGy in 2 fractions over 3 days.	Not reported	**Clearance of haematuria:** 59% (13/22) 2-fraction, 16% (3/19) conventional **Improvement of pain:** 73% (16/22) 2-fraction, 37% (7/19) conventional RT. Disease was fatal in all patients **Overall survival:** Mean 9.77 months 2-fraction vs 14.47 months conventional		No pain data for 7 patients.
Jose (1999) UK	Observational study (appears prospective) 1988-1992	65 patients over 70yrs with MIBC who were not suitable for standard radical radiotherapy regimen of 64Gy in 32 fractions over 6.5wks.	<table><tr><td></td><td></td></tr><tr><td>Median age</td><td>81</td></tr><tr><td>Age range</td><td>71-95</td></tr><tr><td>Male</td><td>38</td></tr><tr><td>Female</td><td>27</td></tr><tr><td>TCC</td><td>63</td></tr><tr><td>Squamous cell</td><td>2</td></tr><tr><td>G2</td><td>20</td></tr><tr><td>G3</td><td>42</td></tr></table>	Weekly 6Gy, total dose 30-36 Gy in 5/6 fractions when treatment intent was local control of disease. Treatment terminated at 12-24 Gy in 10 pts when aim was palliation.	N/a	Median 29 months (range 20-70)	**Overall survival:** Median survival 35 weeks, 2-yr survival 21%. 37 (62%) achieved complete response (6 of these relapsed locally and 1 both locally and with mets). **Symptom control:**		Outcomes not reported separately for patients treated for local control and those treated for palliation.

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			Gx: 3 Dose (Gy) 36: 30 30: 25 24: 5 18: 3 12: 2 54 patients had T3 or T4 disease, 6 had distant mets.				Haematuria controlled in 7/14 (50%) and frequency in 10/16 (63%), dysuria 3/10 (38%), nocturia 1/27 (5%) **Toxicity:** 23 (36%) acute bowel toxicity, 40 (63%) acute bladder toxicity. 1 urinary obstruction (RTOG grade 4). 7/16 (44%) late bladder morbidity, 1 (6%) late rectal morbidity.		
McLaren (1997) UK	Retrospective review Study period not reported	55 patients unsuitable for radical treatment due to poor performance status, comorbid illness, or tumour stage.	Median age: 78 Male: 45 Female: 20 WHO PS 0: 0 WHO PS1: 18 WHO PS 2: 34 WHO PS 3: 13 WHO PS 4: 0 T2: 34 T3: 24 T4a: 7 N0: 63 N1: 2 M0: 61 M1: 4 G1: 0 G2: 29 G3: 36	Patients treated supine using a ct planned volume. The empty bladder and perivesicular tissues incorporated with a 1.5cm margin, typical treatment volume 1000cm^3. 10MV linear accelerator using open anterior and 2 wedged postero-oblique fields. Hyperfractionated schedule. Once weekly 6Gy fractions to 100% isodene as target minimum to 30Gy and 36Gy	N/a	Median follow-up for those still alive was 18mo (range 5-41)	**Palliation from symptoms:** At 1-mo post-RT review 28/55 (51%) were completely palliated from symptoms. 7 (13%) noticed improvement in urinary symptoms. In total 73% were asymptomatic or experienced an improvement in symptom control 1 month from RT. 17 (26%) failed to benefit from treatment – 10 worsening urinary symptoms, 7 persistent bowel symptoms. **Toxicity:** 28 (43%) worsening of symptoms – 12 urinary toxicity, 9 bowel toxicity, 7 bowel		

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							and urinary toxicity. 8 (125) required inpatient admission for toxicity, **Survival:** 52 deaths, median survival 9mo, range 0-41.		
Holmang (1996) Sweden	Retrospective cohort study 1981-1992	96 patients unfit for cystectomy, full-dose RT, or CT treated with short course pelvic RT.	T2M0: 13 T3M0: 36 T4M0: 26 T2-T4 M+: 21 Median age: 80 (51-90) Ureteral obstruction: 14 unilateral, 24 bilateral haematuria: 14 Severe local symptoms: 17	RT generated by 8MV, 11 MV, 16 MV linear accelerator, 2-field technique. 15 patients treated with 5 Gy, 4 times to max 20Gy, 81 treated with 7 Gy, 3 times total 21 Gy. Treatment every 2 days.	n/a		**Median survival:** 6 months. 4 alive with no evidence of disease min 44 mo (T2-T3M0). **Early side effects** 25 severe GI/bladder 22 of these hospitalised for median 10 days. Side effects in 20 other patients who were already under care at hospital or nursing home. **Treatment-related mortality:** n=5 **Symptom relief:** 17 had severe local symptoms before treatment. No patients improved after RT. (however 10/17 died with 4 mo and 2 treated with ureteral catheters).		
Salminen 1992 Australia	Retrospective review 1983-1985	94 locally advanced, recurrent or metastatic BCa treated with external RT for palliation of local disease. Excluded prior	Median age: 79y (55-92) Male: 69 (73%) Female: 25 (27%) Haematuria: 85% N+: 15 (16%) M+: 15 (16%) Nx: 42 T2: 33 (35%) T3: 24 (26%)	Megavoltage beams from 4 or 6 MeV linear accelerator. Total mid point dose 30Gy in 6 fractions, 2 fractions/week at least 2 days apart over 3 weeks. 86% treated with 2	n/a		**Symptom relief:** 40 (43%) complete relief, 29% partially resolved symptoms. 8/17 patients with catheter prior to RT did not need it after RT. **Survival:** Median survival 9.6 months. 29%		

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		pelvic RT.	T4: 30 (32%) Hydronephrosis: Unilateral 27 Bilateral 6 Indwelling catheter before RT: 17 (18%)	opposed anterior and posterior fields. 11 patients with 3 fields and 2 with 4 fields.			survived at 2 years and 13% at 5 years Median DSS 13.3 mo Median time to progression 8.3 mo **Toxicity:** 15 (16%) grade 3 diarrhoea requiring treatment. 15 (16%) nausea/vomiting, 19 (20%) frequency or incontinence. Late effects >3mo after RT in 27 (29%). Including urethral stricture, proctitis, cystitis, haematuria.		
Spagnoletti (2010) Italy	Retrospective observational study 2006-2009	25 with T2-T4, N0-2 bladder cancer receiving palliative external radiotherapy	21 males, 4 females presented with haematuria and local pain and their medical condition or disease status prevented an operation or radical therapy. Mean age 77 (range 63-87)	Different fractionation schedules were used: conventional irradiation 20-30 fractions up to 40-54GY in 16 cases and hypofractionated RT with 1-3 fractions of 6-10 Gy once a week in 9 cases. Treatment with 3 or 4 10-18 MV photon beams.	n/a		**Symptom relief:** Haematuria improved 13/17 patients (76.5%). Pain and /or dysuria improved decreased in 5/12 (41.7%). Mean duration of response 17 weeks (3-118). Complete haematuria clearing 2/9 (22%) with conventional fractionation and 4/8 (50%) in hypofractionated group. 6Gy were least useful treatments, up to 3 fractions only a slight benefit observed. **Toxicity:** No significant difference in toxicity between two schedules.		Abstract only

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							12 (47%) acute genitourinary toxicity. No significant late toxicity **Overall survival:** 24% at 1-year and 12% at 2 yrs. Mean survival 32 weeks (range 4-120)		
Saunders 2006 UK	Retrospective review	43 bladder cancer patients receiving palliative radiotherapy	9 Node positive, 9 T4 disease, 12 had a performance status of 3. Median age 85 (range 70-92).	All treated using anterior-posterior parallel-opposed fields with a mid plane dose of 20Gy in 5 fractions (n=36) or 8 Gy single fraction (n=7). 16 had RT planned using a standard 2D simulator based on bony landmarks. 27 patients were planned using 3D virtual simulation with fields encompassing the bladder with a margin of 1.5-2cm	2D versus 3D virtual simulation planning	Not reported	**Overall survival:** Median OS =6 months for male and 13 months for male (sic) patients. 12 month OS 31%. Use of virtual simulation did not alter survival but did demonstrate a trend towards decreased treatment volumes for female patients and increased treatment volumes for male patients.		Abstract only
Wijkstrom 1991 Sweden	Observational study 1974-1986	162 patients not fit enough for radical treatment who received palliative radiotherapy	Mean age: 78 (range 54-96) Men: 94 Female: 68 Primary tumour: 103 Recurrent: 59 T1: 19 T2: 32 T3: 73 T4: 34	Short term radiotherapy (7Gy 3 times a day over 5 days) total dose 21 Gy. 8MeV photons were used from anterior and posterior opposing fields with a 12x15cm field size.	N/a	Not reported	**Survival:** Patients who responded to RT had a relative 5-yr survival of 58% compared to 4% in those who failed to respond. No difference in survival for age, gender, grade or primary/recurrent tumour.		Endoscopic check impossible in 57 (35%) patients. Data on side effects lacking in 64 patients

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				In 8 patients RT was repeated 6-12mo later and 1 patient received 3 courses of 21 Gy No consistent screening for metastases was attempted Indications for RT was cure in 85 patients (advanced age or ill health), bleeding in 52 and local symptoms in 25.			For patients considered to be curable 5-yr survival was 21% compared with 6% for bleeding and 0% for other symptoms. **Palliation:** improvement in tumour-associated symptoms noted in 75 patients. 27 showed improvement in bleeding, Severe local symptoms improved or disappeared in 14/25 patients. Results hard to assess due to insufficient information. **Complications**: 68/162 (42%) suffered acute side effects but usually minor. Late serious complications in 5 (3%) patients.		
Kouloulias 2013 Greece	Prospective observational study 2005-2011	58 patients with organ-confined (cT1-2, N0) bladder cancer. All inoperable, with poor PS, >75yrs. Excluded previous pelvic RT or cystectomy, LN mets, distant mets or hip prosthesis.	Median age: 77 (70-91) T1: 12 T2: 46 PS 60-70%: 10 PS 50-60%: 48 Male/female: 47/11	Hypofractionated 3DCRT- virtual CT planning used. Clinical target volume (the bladder) and planning target volume obtained by expanding CTV with a margin of 1cm in each direction and of 0.5cm posteriorly. Entire bladder was treated using 4-field technique with 15	N/a	3 months after RT treatment	**Acute Grade 1-2 GI toxicity:** 13/58 (22%) **Acute Grade 1-2 GU toxicity:** 19/58 (33%) No grade 3 or higher GI or GU toxicity. **Patient-reported pain:** VAS score improved from 4.2 (±1.1) to 1.8 (±0.6) ($p<0.001$). **Palliation of haematuria:** 55/58 (94.8%). **Progression-free survival:** Median 14		Also in evidence review for topic L2. Data very unclear. Unsure if rates refer to patients with or without symptom palliation before and after treatment.

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				MV x-ray energy beams. 36Gy in 6 weekly fractions.			months		