Adaptive radiotherapy for bladder cancer – a systematic review

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Table 1. Studies reporting the use of adaptive strategies for bladder radiotherapy

Reference; No. patients;	Adaptive Strategy	Bladder protocol	CTV	PTV generation	Evaluation Metrics	Findings
Burridge 2006 [9]; N= 20	POD – SI	Empty	Whole bladder	Standard PTV: Bladder + 15 mm POD-PTVs: Bladder + 15 mm in RLAPI, S: 5mm, 10mm	Small bowel	↓ small bowel irradiation
Vestergaard 2010 [10]; N=10	POD – SI POD – MI	Empty	Bladder & PLN	Standard PTV: CTV + A(25mm), P(20mm), RL(15mm), S(28mm), I(18mm) POD-PTV method 1: Small, medium and large expanded by margin that cover 50, 70, 90% of population + 3mm POD-PTV method 2: Small = CTV + 8mm. Medium = CTV + margin scaled according to the location frequency of CTV in the first 5 CBCTs. Large = CTV + 23mm AS, 18mm P, 13mm RLI. POD-PTV method 3: Small = Combination of 2 smallest CTV + 3mm from planning CT + first 5 CBCTs. Medium = combo of 5 CBCT CTVs + 3mm. Large = CTV + 23mm AS, 18mm P, 13mm RLI.	Volume receiving specific dose	↓ volume by 30-40% POD-PTV method 1 recommended due to much simpler process but equivalent efficacy with the other two
Tuomikoski 2011 [11]; N=5	POD – MI	Empty	Bladder & tumor	Standard PTV: CTV + 20mm POD-PTV: CTV + 15mm RLIP and various AS margin (5, 10, 15, 20mm)	Volume receiving specific dose Small bowel dose Target coverage	↓ small bowel irradiation Equivalent target coverage as standard
Lalondrelle 2011[12]; N=15	POD – MI	Empty	Bladder	Standard PTV: CTV + 15mm POD-PTV: 1) CTV on CT acquired 15 mins after first scan + 15mm; 2) CTV on CT acquired 30 mins after first scan + 15mm	Target coverage	Target coverage improved from 51% to 96^ by use of POD-PTV
Foroudi 2011 [13]; N=27	POD – MI	Empty	Bladder	Standard PTV: CTV + 15mm POD-PTV: Small – Smallest of the 6 CTVs from Planning and Fx 1-5 CBCTs + 5mm; large CTV: Combination of all 6 CTVs + 5mm; medium CTV: Half way between small and large	Volume receiving 45Gy (V_{45}) and 5Gy (V_5) Target coverage	↓V_{45} and V_5 by 29% and 15% with equivalent target coverage with Standard

Reference; No. patients;	Adaptive Strategy	Bladder protocol	CTV	PTV generation	Evaluation Metrics	Findings
Murthy 2011 [14]; N=10	POD – SI	Full/Empty depending on location of CTV	Bladder	POD-PTV: CTV + isotropic margin from 5 – 30mm in 5mm increments	Target coverage Frequency of PTV selected	Target coverage achieved with PTV with margin expansion of 5 – 15mm
Kuyumcian 2012 [15]; N=27	POD – MI	Empty	Bladder	Standard PTV: CTV + 15mm POD-PTV: Small – Combination of the two smallest CTVs from Planning and Fx 1-5 CBCTs + 5mm; large CTV: Combination of all 6 CTVs + 5mm; medium CTV: Half way between small and large	Frequency of PTV selected	Better distribution of PTV selected
Meijer 2012 [16]; N=20	POD – MI	Full	Bladder & tumor	POD-PTVs: 6 generated based on interpolation and extrapolation of the full bladder and empty bladder acquired with two scans	Qualitative evaluation on dose Toxicity	↓ dose to small bowel No Grade 3 toxicity
McDonald 2013 [19]; N = 25	POD – MI	Empty	Bladder	Standard PTV: CTV + 15mm POD-PTV: Small – CTV + 5mm; medium – CTV + 15mm AS, 10mm P, 5 RLI; large – CTV + 20mm A, 12mm P, 7.5mm RL, 25mm S, 7.5mm I for patient with slow filling. Patient with fast filling, large POD-PTV expanded by 15mm AS, 10mm P and 5mm RLI on CTV on CT acquired 30 mins after first scan	Target coverage Normal tissue sparing Frequency of PTV selected	Target coverage of 96% ↑ normal tissue sparing 49% and 45% delivered using small and medium PTV
Vestergaard 2014 [20]; N=20	POD – MI	Empty	Bladder; 13 with PLN	Standard PTV: Bladder + A(25mm), P(20mm), RL(15mm), S(28mm), I(18mm) POD-PTV: Small = Combination of 2 smallest CTV from planning CT and first 4 CBCTs + 8mm. Medium = combo of 5 CTVs + 8mm. Large = Standard PTV	Volume Dose to small bowel and rectum	↓ volume by 30% ↓ dose to small bowel and rectum Less sparing when PLN was included in treatment volume

Reference; No. patients;	Adaptive Strategy	Bladder protocol	CTV	PTV generation	Evaluation Metrics	Findings
Vestergaard 2014 [21]; N=13	POD – MI	Empty	Bladder	Standard PTV: Bladder + A(25mm), P(20mm), RL(15mm), S(28mm), I(18mm) POD-PTV method 1: Small = Combination of 2 smallest CTV from planning CT and first 4 CBCTs + 8mm. Medium = combo of 5 CTVs + 8mm. Large = Standard PTV POD-PTV method 2: Small, medium and large = CTV + 5mm + margin covering 33%, 67% and 99% percentile, respectively of the DVF generated from the 4 CT-CBCT DIR	Volume	DVF-based POD recommended (↓ volume by 36%)
Tuomiskoski 2015 [22]; N = 10	POD – MI	Empty	Bladder	CT-based POD: 4 PTVs generated by expanding 8mm on 4 CTVs on CTs acquired at every 15 minutes CT-CBCT based POD: Small – 2 smallest CTV from CT and first 4 CBCTs + 8mm; medium – Combination of 5 CTVs + 8mm; large – CTV from CT + A(25mm), P(20mm), RL(15mm), S(28mm), I(18mm)	Volume Frequency of PTV selected	Greater volume reduction by CT-based POD than CT-CBCT based POD More adequate range of PTV in CT-CBCT based POD
Lutkenhaus 2015 [23]; N=8	POD – MI	Full	Bladder + PLN	Standard PTV: CTV + 13mm AS, 7mm RLPI 5 PTVs derived based on scaling of DVF generated from full bladder CT-empty bladder CT DIR registration to represent 0, 33%, 67%, 100% and 133% bladder filling states	Target coverage Dose to rectum and bowel	99% target coverage Significant reduction of bowel volume receiving 30Gy and 40Gy
Vestergaard 2013 [18]; N=7	POD – MI & ReOpt	Empty	Bladder + PLN	Standard PTV: Bladder + A(25mm), P(20mm), RL(15mm), S(28mm), I(18mm) POD: Small = Combination of the two smallest bladder from first 4 CBCTs + 3mm; Medium = Combination of all 4 CBCT bladders + 3mm. Large: Standard PTV ReOpt: Daily bladder on CBCT + 5mm	Volume receiving specific dose level	ReOpt significantly better than POD in volume sparing

Reference; No. patients;	Adaptive Strategy	Bladder protocol	CTV	PTV generation	Evaluation Metrics	Findings
Pos 2006 [26]; N=21	PS-PTV	Full	Tumor (Partial bladder)	Standard: Bladder + 20mm PS-PTV: Bladder from Fx 1-5 + 10mm	$PTV_{Planned}$ Target coverage	PTVPlanned ↓40% 95% target coverage
Foroudi 2009 [27]; N=5	PS-PTV	Empty	Bladder	Standard: Bladder + 15mm PS-PTV: Average bladder from Fx 1-5 CBCT + 15 mm	Minimum dose to CTV	↑ dose to CTV / target coverage
Tolan 2011 [25]; N = 11	PS-PTV	Full	Bladder	Standard: Bladder + 20mm PS-PTV: 1) Occupancy Volume (OV): Bladder from 15 CBCTs; 2) OV + 5mm; 3) Measurement-based PS-PTV (mPS-PTV)	$PTV_{Planned}$ Target coverage	OV + 5mm recommended due to equivalent coverage achieved with mPS-PTV but smaller volume
Webster 2013 [17]; N=20	PS-PTV POD – SI	Empty	Bladder	Standard: Bladder + 15mm 4 POD-PTVs: Bladder + 15mm in RLAPI, S: 5, 10, 15, 20mm PS-PTV: 1) Bladder from first 3 CBCTs + 5mm; 2) Bladder from first 3 CBCTs + 10mm	$PTV_{Planned}$ Target coverage	POD recommended due to better target coverage

Abbreviations: N = number. CTV: Clinical Target Volume. POD-SI: Plan of the Day based on single image. POD-MI: Plan of the Day based on multiple images. ReOpt: Daily ReOptimization. PS-PTV: Patient-specific PTV. R: Right. L: Left. S: Superior. I: Inferior. A: Anterior. P: Posterior. Fx: Fraction. DVF: Deformation Vector Field. DIR: Deformable Image Registration. $PTV_{Planned}$: PTV averaged over the course of treatment