

Expanding Role of SBRT in Primary Bladder Cancer – Is It Ready for Prime Time?

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Abstract: Muscle invasive bladder cancer (MIBC) is treated by either radical cystectomy followed by adjuvant therapy or bladder preservation approach with radical chemoradiation (CTRT) after maximal safe resection of bladder tumor (TURBT). However, a substantial proportion of patients either develop toxicities or are in poor performance status for radical CTRT. MIBC on the other hand remains extremely symptomatic with pain, bleeding and eventually irritative/obstructive bladder symptoms and disease progression. Stereotactic body radiotherapy (SBRT) evolved as a curative option in many disease sites and gained popularity as a curative intent treatment in oligometastatic disease scenarios. SBRT targeting macroscopic bladder tumor with shorter treatment course, optimisation of symptom (eventual tumor) control and better compliance led to exciting albeit few publications. This review will highlight role of SBRT in primary bladder cancer.

Keywords: Bladder cancer; SBRT; Image-Guided Radiation Therapy (IGRT); Toxicity.

SBRT proved its clinical effectiveness in several cancers as curative (early-stage lung, liver, prostate) or effective palliative (brain/spine metastases) means over the last decade or so^[1]. The ever-expanding horizon ushered into oligometastatic disease scenario as well after available randomized clinical data such as SABR-COMET^[2]. The clinical application of SBRT in bladder cancer especially non metastatic MIBC remained a slow development. The inherent challenges of bladder preservation against radical cystectomy, associated myths and belief system for non surgical methods reduced its wider acceptance^[3]. However the role of palliative radiotherapy for symptom control has long been proved effective. The inherent nature of bladder radiosensitivity, bowel toxicity and techniques effective for safe delivery were hindrance to clinical application of SBRT in MIBC or oligometastatic bladder cancer (OMBC). The whole bladder is conventionally considered as the target volume due to the difficulties in tumor localization, in the accuracy of treatment delivery, and because bladder cancer is usually multifocal^[4]. Weekly once delivery allowed for recovery of acute toxicity and also no deleterious effect in outcome^[5]. SBRT in limited volume OMBC in Italian series showed promising results with low rate of acute toxicity^[6].

It is interesting to explore SBRT in bladder cancer in two unique clinical scenarios, application in chemotherapy unsuitable cohort in MIBC and in OMBC. Categorization of OMBC was based on the timing of occurrence in relation to the diagnosis of MIBC, treatment of the primary tumor, and administration of sys-

temic therapy. There was unanimity on the categories and their definition. All studies and the review used the following categories viz. synchronous, oligorecurrence and oligoprogression^[7]. There are rather limited data in MIBC for the use of SBRT. Traditionally MIBC patients if opted for non-surgical method, receives long course chemoradiation or moderate hypofractionated RT with chemotherapy^[8,9]. Unfortunately there is still no concrete evidence for bladder SBRT in amendment of ASCO-AUA-ASTRO guidelines or rather radiotherapy alone (even with SBRT) been cited as inferior treatment^[8]. The available literature about hypofractionated radiotherapy schedule been listed in Table 1^[10]. The two series from Italy addressed SBRT schedules in weekly once protocol and with acceptable range of toxicities. The symptom control was very high and this kind of paved pathways for future protocols^[11,12].

With the advent of immunotherapy new generation trials are testing combination of SBRT with immunotherapy. Trimodality therapy with external beam long course RT replaced by SBRT and chemotherapy replaced by immunotherapy been tested and Kundu et.al reported the safety protocol in ASCO GU 2022^[13]. In this protocol SBRT 33 Gy/5 fractions was given between 1st and 2nd cycle of dual immunotherapy agents (Durvalumab and Tremelimumab). With only 10 patients the reported local control was 90%. This will surely guide in future application of bladder SBRT. The synergistic effect of immunomodulatory action by SBRT and immunotherapy holds promise. The lack of phase 3 data remains a deterrent in prime-time application of bladder SBRT.

Huddart et.al reported their phase 2 data with MIBC not suitable for long course CTRT or radical cystectomy. A plan of the day approach was utilised and image guidance protocol were maintained. Weekly 36 Gy/6 fractions to whole bladder (empty)

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Table 1. Hypofractionated Bladder RT schedules.

Study Design	Fractionation	Stage	Symptom Control	Toxicity Reported	Response/Tumor Control
Ali et.al. ^[14] -Retrospective	8 Gy/SF – 30 Gy/10 fractions	T1-4N1-3M0-1	Hematuria- 54% Pain-48%	NR	NR
Duchesne et al. ^[15] - RCT	35 Gy/10 fractions Vs 21 Gy/7 fractions	T2-4N0-1M0-1	Hematuria-88% Pain-NRDysuria/ Frequency-70%	Bladder/bowel grade 2 +: 30%	NR
McLaren et.al. ^[16] - Prospective	30-36 Gy/6 fractions	T2-4N0-1M0-1	Hematuria-92% Dysuria/ Frequency-52%	Urinary-18%. Bowel-8% (more than Grade 2)	NR
Kouloulis et al. ^[17] - Prospective	36 Gy/6 fractions	T1-2N0M0	50-63% (Details NR)	0% more than Grade 2	NR
Dirix et al. ^[12] -Prospective	34.5 Gy/6 fractions	T1-4N1-3M0-1	Hematuria-90%	Bladder-9% (> Grade 2)	NR
Zygiogianni et al. ^[18]	36 Gy/6 fractions			2.3% acute	NR
Hafeez et al. ^[19]	36 Gy/6 fractions			22% acute Grade 3	2 years Local control 83%

SF, Single fraction; NR, not reported; RCT, randomized controlled trial.

was delivered. With median age of patients being 86 years, this protocol proved to be safe in terms of genitourinary (GU) and gastrointestinal (GI) acute grade 3 toxicity of 18% and 4% respectively. The local control was excellent and only 7% at 1 year had local progression^[20]. This study also highlighted the fact that geriatric population often deemed as unsuitable for radical treatment can safely be considered for bladder SBRT. And the daily image guidance and choosing the plan of the day approach reduced GU and GI toxicities. In a similar manner Alati et.al. reported geriatric MIBC receiving TMT with twice daily hypofractionated radiotherapy. The data reported 70% 5 years survival with bladder preserved and established against the notion for radical treatment in geriatric age group. Future studies should test between this regimen with SBRT for MIBC^[21]. In recent times Fossa et.al also published their preliminary experience of bladder SBRT among elderly and frail patients highlighting the safety and efficacy^[4,22].

The technical considerations for SBRT for any sites need careful planning and execution. Two very important points besides several others are dose and planning target volume (PTV) in MIBC. Since dose has been discussed previously, let us highlight on PTV. Departments following bladder preservation should advocate daily image guidance and a plan of the day approach seems reasonable^[23–25]. The PTV creation depends upon bladder filling capacity while delivering the treatment. The complexity of

choosing the margins been enumerated by Murthy et.al. over last decade across several publications and similarly by Huddart et.al.

Future bladder SBRT protocols should encompass the following key points:

1. Incorporation of daily image guidance and choosing the optimal plan.
2. Motion management strategies like plan/PTV of the day approach.
3. Weekly once protocol.
4. Consideration of partial bladder SBRT.
5. Incorporation of immunotherapy with SBRT.
6. A randomised data between long course IGRT versus SBRT weekly once.
7. Incorporation of MRI guided treatment delivery- real time adaptation.

With the evolving landscape of managing MIBC and OMBC by combination of immunotherapy and radiotherapy, the International Geriatric Radiotherapy group guidelines (IGRG) provide a comprehensive literature related to several clinical aspects of bladder preservation and different dose fractionations available. Bladder preservation and that too by SBRT remains an art and science worth exploring^[25]. The available literature and sparse reporting of either local control or toxicities have been enumerated in [Table 1](#). Here we also shared our initial experience of treating MIBC and OMBC with SBRT in [Table 2](#).

Table 2. Initial experience Bladder SBRT-Our Institute.

Patient Number	Case Scenario	Dose/Fractionation	Symptom Control	Toxicity Reported	Response/Tumor Control
1	MIBC-89 years/M	36 Gy/6 fractions/ Weekly once	Hematuria- 90%	Grade 2 cystitis Grade 2 lower GI	NR
2	OMBC-65 years/F	30 Gy/5 fractions/ Weekly once	Hematuria-60% Pain-50%	Grade 3 GU-Hematuria @ 6 months post SBRT	Died @ 9 months post SBRT-Metastatic progression
3	MIBC-88 years/M	36 Gy/6 fractions/ Weekly once	Hematuria-90% Dysuria/Frequency-70%	Grade 2 GI/GU	NED @ 3 months post SBRT
4	MIBC-54 years/M	36 Gy/6 fractions/ Weekly once	Hematuria-50%	Cystitis Grade 2 Diarrhoea Grade 2	2 months post SBRT- Clinically controlled
5	MIBC-84 years/M	30 Gy/5 fractions/ Weekly once	Hematuria-90%	Cystitis Grade 1	1 months post SBRT- clinically controlled

MIBC, Muscle invasive bladder cancer; OMBC, Oligometastatic bladder cancer; NED, No evidence of disease.

Conclusion

With advances in SBRT protocols across different disease spectrum and sites, bladder SBRT lagging due to limited data and often exclusion from treatment due to age group. Modern plan of the day IGRT based SBRT and incorporation of immunotherapy will answer many questions related to bladder SBRT. The definition also requires further research between covering whole bladder versus tumor only SBRT. Eventually clinical decision making by choosing wisely remains the most important factor. Till that time bladder SBRT remains a potential yet challenging treatment modality which should be practiced under stringent multidisciplinary team work and we are yet to conclusively say that it is ready for prime time.

Abbreviations

IGRT, image guided radiotherapy; MIBC, muscle invasive bladder cancer; NED, no evidence of disease; OMB, oligometastatic bladder cancer; SBRT, stereotactic radiotherapy.

Authors' contributions

TB: data collection, analysis, literature review, JPS: literature review, drafting, SJK, RRM, AUG, GKR: Literature review. All authors contributed to the article and approved the submitted version.

References

- [1] Alongi F, Arcangeli S, Filippi AR, et al. Review and uses of stereotactic body radiation therapy for oligometastases. *Oncologist*, 2012, 17(8): 1100-1107.
- [2] Palma DA, Olson R, Harrow S, et al. Stereotactic Ablative Radiotherapy for the Comprehensive Treatment of Oligometastatic Cancers: Long-Term Results of the SABR-COMET Phase II Randomized Trial. *J Clin Oncol*, 2020, 38(25): 2830-2838.
- [3] Elumalai T, Joseph N, Choudhury A. Myths About Bladder Preservation in Muscle-Invasive Bladder Cancer. *Semin Radiat Oncol*, 2023, 33(1): 56-61.
- [4] Jereczek-Fossa BA, Marvaso G. Palliative radiation therapy in bladder cancer: a matter of dose, techniques and patients' selection. *Ann Palliat Med*, 2019, 8(5): 786-789.
- [5] Pos FJ, Hart G, Schneider C, et al. Radical radiotherapy for invasive bladder cancer: What dose and fractionation schedule to choose? *Int J Radiat Oncol Biol Phys*, 2006, 64: 1168-1173.
- [6] Augugliaro M, Marvaso G, Ciardo D, et al. Recurrent oligometastatic transitional cell bladder carcinoma: is there room for radiotherapy? *Neoplasma*, 2019, 66: 160-165.
- [7] Bamias A, Stenzl A, Zagouri F, et al. Defining Oligometastatic Bladder Cancer: A Systematic Review. *Eur Urol Open Sci*, 2023, 55: 28-37.
- [8] Holzbeierlein J, Bixler BR, Buckley DI, et al. Treatment of Non-Metastatic Muscle-Invasive Bladder Cancer: AUA/ASCO/SUO Guideline (2017; Amended 2020, 2024). *J Urol*, 2024, 212(1): 3-10.
- [9] Hall E, Hussain SA, Porta N, et al. Chemoradiotherapy in Muscle-invasive Bladder Cancer: 10-yr Follow-up of the Phase 3 Randomised Controlled BC2001 Trial. *Eur Urol*, 2022, 82(3): 273-279.
- [10] Perera J, Hoskin P. The role of radiotherapy in metastatic bladder cancer. *J Cancer Metastasis Treat*, 2022, 8: 4.
- [11] Kouloulis V, Tolia M, Kolliarakis N, et al. Evaluation of acute toxicity and symptoms palliation in a hypofractionated weekly schedule of external radiotherapy for elderly patients with muscular invasive bladder cancer. *Int Braz J Urol*, 2013, 39: 77-82.
- [12] Dirix P, Vingerhoedt S, Joniau S, et al. Hypofractionated palliative radiotherapy for bladder cancer. *Support Care Cancer*, 2016, 24: 181-186.
- [13] Kundu P, Lee A, Drakaki A, et al. Safety lead-in of phase II SBRT and durvalumab with or without tremelimumab for unresectable and cisplatin-ineligible, locally advanced or metastatic bladder cancer. *J Clin Oncol*, 2022, 40: 517-517.
- [14] Ali A, Song YP, Mehta S, et al. Palliative Radiation Therapy in Bladder Cancer-Importance of Patient Selection: A Retrospective Multicenter Study. *Int J Radiat Oncol Biol Phys*, 2019, 105(2): 389-393.
- [15] Duchesne GM, Bolger JJ, Griffiths GO, et al. A randomized trial of hypofractionated schedules of palliative radiotherapy in the management of bladder carcinoma: results of medical research council trial BA09. *Int J Radiat Oncol Biol Phys*, 2000, 47(2): 379-388.
- [16] McLaren DB, Morrey D, Mason MD. Hypofractionated radiotherapy for muscle invasive bladder cancer in the elderly. *Radiother Oncol*, 1997, 43(2): 171-174.
- [17] Koukourakis G, Kouloulis V, Zacharias G, et al. Therapeutic interventions targeting organ preservation in muscle-invasive bladder cancer: a review. *Clin Transl Oncol*, 2011, 13(5): 315-321.
- [18] Zygogianni A, Kouloulis V, Armpilia C, et al. A weekly hypofractionated radiotherapeutic schedule for bladder carcinoma in elderly patients: local response, acute and late toxicity, dosimetric parameters and pain relief. *J Buon*, 2013, 18(2): 407-412.
- [19] Hafeez S, McDonald F, Lalondrelle S, et al. Clinical Outcomes of Image Guided Adaptive Hypofractionated Weekly Radiation Therapy for Bladder Cancer in Patients Unsuitable for Radical Treatment. *Int J Radiat Oncol Biol Phys*, 2017, 98(1): 115-122.
- [20] Huddart R, Hafeez S, Lewis R, et al. Clinical Outcomes of a Randomized Trial of Adaptive Plan-of-the-Day Treatment in Patients Receiving Ultra-hypofractionated Weekly Radiation Therapy for Bladder Cancer. *Int J Radiat Oncol Biol Phys*, 2021, 110(2): 412-424.
- [21] Alati A, Fabiano E, Geiss R, et al. Bladder preservation in older adults with muscle-invasive bladder cancer: A retrospective study with concurrent chemotherapy and twice-daily hypofractionated radiotherapy schedule. *J Geriatr Oncol*, 2022, 13(7): 978-986.
- [22] Marvaso G, Vitullo A, Corrao G, et al. Muscle-invasive bladder cancer in elderly and frail people: Is hypofractionated radiotherapy a feasible approach when no other local options are available? *Tumori J*, 2024, 110(3): 193-202.
- [23] Murthy V, Master Z, Adurkar P, et al. 'Plan of the day' adaptive radiotherapy for bladder cancer using helical tomotherapy. *Radiother Oncol*, 2011, 99(1): 55-60.
- [24] Krishnan A, Maitre P, Kashid S, et al. Online Adaptive Radiotherapy for Bladder Preservation: Transitioning to Hypofractionation. *Int J Radiat Oncol Biol Phys*, 2025.
- [25] Nguyen NP, Karlsson UL, Page BR, et al. Immunotherapy and radiotherapy for older patients with invasive bladder cancer unfit for surgery or chemotherapy: practical proposal by the international geriatric radiotherapy group. *Front Oncol*, 2024, 14: 1371752.