



# Editorial: The Evolving Landscape of Stereotactic Body Radiation Therapy for the Management of Prostate Cancer

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## Editorial on the Research Topic

### The Evolving Landscape of Stereotactic Body Radiation Therapy for the Management of Prostate Cancer

Over the last decade, an increasing number of publications have demonstrated the feasibility, safety, and efficacy in utilizing a condensed schedule of radiation to manage localized prostate cancer (1–4). Hypofractionation refers to delivering modestly larger doses than is prescribed with conventional regimens, while ultrahypofractionation refers to delivering an even larger dose with correspondingly fewer fractions. Stereotactic Body Radiation Therapy (SBRT) is the technique utilized to deliver ultrahypofractionation, and has become a standard regimen employed in the treatment of men with low and intermediate risk prostate cancer. This Research Topic highlights the evolving landscape of Stereotactic Body Radiation Therapy for the management of localized and advanced prostate cancer, addressing current data regarding clinicopathologic and dosimetric optimization with novel perspectives.

Numerous prospective phase I/II studies have shown favorable biochemical outcomes with the use of prostate SBRT (5–16). A study comprised of pooled single and multi-institutional trials from a cohort of 2142 patients demonstrated excellent 7-year biochemical outcomes for men with low, favorable intermediate, and unfavorable intermediate risk disease (17). A meta-analysis composed of over 6,000 patients highlighted the prospective evidence supporting the use of SBRT, concluding, “SBRT has sufficient evidence to be supported as a standard treatment option for localized prostate cancer while ongoing trials assess its potential superiority (18)”. Based on data from the NCCN and SEER database, there has been a contemporaneous increase in the use of SBRT for managing localized prostate cancer (19–22).

While most of the initial publications involving the use of prostate SBRT centered on the treatment of men with low and intermediate risk disease, patients with unfavorable intermediate or high risk disease were often times also included. The applicability of SBRT to men with unfavorable intermediate and high risk disease continues to evolve. An increasing number of series have characterized promising biochemical outcomes for this specific cohort (17, 23–26). Reflecting these emerging data, the National Comprehensive Cancer Network (NCCN) begrudgingly supports the use of SBRT for men with unfavorable intermediate or high risk disease “...if delivering longer

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courses of EBRT would present a medical or social hardship (27)". Most recently, the Scandinavian HYPO-RT-PC trial randomized 1200 men with intermediate-risk or high-risk prostate cancer to conventional vs. stereotactic radiotherapy regimens. Eleven percent of the cohort harbored high risk disease. At a median follow-up of 5 years, there was parity in biochemical and late grade 2+ urinary or bowel outcomes (28). Ricco et al. review the literature pertaining to the use of prostate SBRT for men with intermediate and high risk disease and independently validate excellent 7-year biochemical control rates similar to that seen in the HYPO-RT-PC trial. Their findings and summary of data to date further advance the notion that patients with advanced localized disease can benefit from an SBRT approach.

Several series have reported a longer time to PSA nadir with a greater absolute magnitude in biochemical response with SBRT when compared with conventional fractionation. These findings are consistent with higher biological effective dosing, which is also found in brachytherapy. (29–31) There is emerging data which suggests an improvement in biochemical outcomes with SBRT dose escalation (10, 32, 33). Whereas most series have accomplished this with homogeneous dosing on robotic or gantry-based platforms, heterogeneous-dosing methods employing a virtual HDR-brachytherapy approach with ablative dosing, has been described, with favorable biochemical and quality of life results (34). Fuller et al. reviews this technique with two different dosing schemas. With both doses, favorable biochemical outcomes were obtained, with modest rates of low toxicity. Given a measurable differential in the absolute magnitude of PSA ablation and quality of life outcomes between dose arms, the authors suggest the ability to utilize age and baseline clinicopathologic features to select between these doses when utilizing this approach.

With the increased utilization of prostate SBRT, there were concerns regarding its use portending for a potential decrease in quality of life. One series explored an increase in genitourinary toxicity through querying Medicare claims data (35). Another analysis had similar findings using data gleaned from the SEER database (20). Since, several series have reported highly favorable patient and physician-reported quality of life outcomes for patients treated with these abbreviated regimens (9, 17, 36, 37). Favorable quality of life outcomes has been further validated by initial data reported from a phase 3 trial comparing 38 Gy in 5 fractions with 79.2 Gy in 44 fractions (38). The PACE-B study randomized men with localized prostate cancer to treatment with conventional, hypofractionated, or SBRT regimens and had a similar finding of quality of life parity between treatment arms (39). Aghdam et al. report further contribute to our understanding of this subject, concentrating on an older patient cohort receiving prostate SBRT. Their findings illuminate patient characterization of disease, and treatment burden, with a minority reporting high long-term burden for either.

The role of pre-treatment clinical factors for predicting long-term quality of life after prostate SBRT continues to mature. The probability of developing benign prostatic hypertrophy and

being diagnosed with prostate cancer independently increase over time. For patients that fail alpha-1 adrenergic receptor antagonists and/or 5-alpha reductase inhibitor medication, Transurethral Resection of the Prostate (TURP) or a derived variant of this procedure, is often prescribed. The role of pre-treatment TURP portending for genitourinary toxicity post definitive LDR brachytherapy or IMRT has been dismissed in select series (40–43). The data regarding pre-existing TURP after SBRT is currently emerging, with mixed findings that appear dependent, in part, on dose (44, 45). Pepin et al. clarify this question by reporting on long-term outcomes for 47 patients treated with modest SBRT dosing for whom previous TURP predicted for transient hematuria with comparable long-term toxicity to conventionally fractionated regimens.

Several series have characterized intrafraction motion during the course of prostate radiotherapy (46–50). Most prostate SBRT regimens employ anisotropic PTV margins between 3–5mm's. Dose escalated HDR-like SBRT approaches use smaller margins of 0–2 mm, expanded to 5 mm adjacent to actual biopsy or MRI-demonstrated peri-capsular disease only, to minimize the risk of adjacent tissue injury (34). Levin-Epstein et al. characterize inter and intra-fractional prostate motion in 205 patients enrolled on two prospective studies of prostate SBRT. Their findings largely validate current stereotactic approaches which focus on accuracy and precision. Interestingly, inter and intra-fractional prostate displacement did not predict for grade 3+ toxicity.

Despite an increase in the number of series published on prostate SBRT and the corresponding acceleration in its adoption, universally recognized dosimetric predictors of toxicity after prostate SBRT remain elusive, with institutional and prospective trial planning objectives frequently based on BED calculations and legacy dose constraints. Publications centered on dose-volume objectives and quality of life outcomes are in want, with differing endpoints and assessments found in select series (44, 51). Valle et al. apply a sophisticated machine learning technique to assess 910 dosimetric features in predicting grade 2+ genitourinary toxicity for 339 patients treated with prostate SBRT at an academic institution. Their findings validate the use of advanced modeling for toxicity prediction, and highlight the need to incorporate biologic and genomic data in future analyses.

Several series have suggested an improvement in outcomes for men with metastatic prostate cancer with treatment to the primary site, culminating in the recent findings published from the STAMPEDE trial (52–57). There is also emerging data addressing potential benefit of stereotactic radiation directed to sites of oligometastatic disease (58). Adorno Febles et al. provide us with a comprehensive view of the rationale, utilization, and evolving data regarding the use of prostate SBRT and elucidates the potential interplay with systemic therapies for managing advanced disease states. A detailed exploration of SBRT and tumor immunology is explored along with a review of ongoing SBRT trials combined with systemic therapeutics.

As a whole, the current Research Topic aggregates a collection of articles which provide a high-level review of the rationale and evolution of the use of SBRT for the treatment of prostate cancer.

It investigates outcomes involving distinct patient cohorts, techniques, and treatment planning objectives as monotherapy and in concert with systemic therapeutics. Ample data has suggested the ability of prostate SBRT to provide an efficacious substitute for costlier and more invasive and/or inconvenient regimens involving radiation therapy. As our understanding of optimal patient selection, techniques, prescriptions and dose objectives continue to develop, the potential for prostate SBRT to become a universally accepted *preferred* radiation therapeutic approach remains tantalizingly close.

## REFERENCES

- Catton CN, Lukka H, Gu CS, Martin JM, Supiot S, Chung PWM, et al. Randomized Trial of a Hypofractionated Radiation Regimen for the Treatment of Localized Prostate Cancer. *J Clin Oncol* (2017) 35(17):1884–90. doi: 10.1200/JCO.2016.71.7397
- Dearnaley D, Syndikus I, Mossop H, Khoo V, Birtle A, Bloomfield D, et al. Conventional versus hypofractionated high-dose intensity-modulated radiotherapy for prostate cancer: 5-year outcomes of the randomised, non-inferiority, phase 3 CHHiP trial. *Lancet Oncol* (2016) 17(8):1047–60. doi: 10.1016/S1470-2045(16)30102-4
- Koontz BF, Bossi A, Cozzarini C, Wiegel T, D'Amico A. A systematic review of hypofractionation for primary management of prostate cancer. *Eur Urol* (2015) 68(4):683–91. doi: 10.1016/j.eururo.2014.08.009
- Morgan SC, Hoffman K, Loblaw DA, Buyyounouski MK, Patton C, Barocas D, et al. Hypofractionated Radiation Therapy for Localized Prostate Cancer: An ASTRO, ASCO, and AUA Evidence-Based Guideline. *J Clin Oncol* (2018) 36(34):JCO1801097. doi: 10.1200/JCO.18.01097
- King CR, Brooks JD, Gill H, Presti JC Jr. Long-term outcomes from a prospective trial of stereotactic body radiotherapy for low-risk prostate cancer. *Int J Radiat Oncol Biol Phys* (2012) 82(2):877–82. doi: 10.1016/j.ijrobp.2010.11.054
- Lischalk JW, Kaplan ID, Collins SP. Stereotactic Body Radiation Therapy for Localized Prostate Cancer. *Cancer J* (2016) 22(4):307–13. doi: 10.1097/PPO.0000000000000209
- King CR, Freeman D, Kaplan I, Fuller D, Bolzicco G, Collins S, et al. Stereotactic body radiotherapy for localized prostate cancer: pooled analysis from a multi-institutional consortium of prospective phase II trials. *Radiation Oncol* (2013) 109(2):217–21. doi: 10.1016/j.radonc.2013.08.030
- Katz A. Stereotactic Body Radiotherapy for Low-Risk Prostate Cancer: A Ten-Year Analysis. *Cureus* (2017) 9(9):e1668. doi: 10.7759/cureus.1668
- Meier RM, Bloch DA, Cottruz C, Beckman AC, Henning GT, Woodhouse SA, et al. Multicenter Trial of Stereotactic Body Radiation Therapy for Low- and Intermediate-Risk Prostate Cancer: Survival and Toxicity Endpoints. *Int J Radiat Oncol Biol Phys* (2018) 102(2):296–303. doi: 10.1016/j.ijrobp.2018.05.040
- Zelefsky MJ, Kollmeier M, McBride S, Varghese M, Mychalczak B, Gewanter R, et al. Five-Year Outcomes of a Phase 1 Dose-Escalation Study Using Stereotactic Body Radiosurgery for Patients With Low-Risk and Intermediate-Risk Prostate Cancer. *Int J Radiat Oncol Biol Phys* (2019) 104(1):42–9. doi: 10.1016/j.ijrobp.2018.12.045
- Buyyounouski MK, Price RA Jr, Harris EE, Miller R, Tomé W, Scheffer T, et al. Stereotactic body radiotherapy for primary management of early-stage, low- to intermediate-risk prostate cancer: report of the American Society for Therapeutic Radiology and Oncology Emerging Technology Committee. *Int J Radiat Oncol Biol Phys* (2010) 76(5):1297–304. doi: 10.1016/j.ijrobp.2009.09.078
- Freeman DE, King CR. Stereotactic body radiotherapy for low-risk prostate cancer: five-year outcomes. *Radiat Oncol* (2011) 6:3. doi: 10.1186/1748-717X-6-3
- Kang JK, Cho CK, Choi CW, Yoo S, Kim MS, Yang K, et al. Image-guided stereotactic body radiation therapy for localized prostate cancer. *Tumori* (2011) 97(1):43–8. doi: 10.1177/030089161109700109
- Madsen BL, Hsi RA, Pham HT, Fowler JF, Esagui L, Corman J. Stereotactic hypofractionated accurate radiotherapy of the prostate (SHARP), 33.5 Gy in five fractions for localized disease: first clinical trial results. *Int J Radiat Oncol Biol Phys* (2007) 67(4):1099–105. doi: 10.1016/j.ijrobp.2006.10.050

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- Chen LN, Suy S, Uhm S, Oermann EK, Ju AW, Chen V, et al. Stereotactic body radiation therapy (SBRT) for clinically localized prostate cancer: the Georgetown University experience. *Radiat Oncol* (2013) 8:58. doi: 10.1186/1748-717X-8-58
- Katz AJ, Santoro M, Diblasio F, Ashley R. Stereotactic body radiotherapy for localized prostate cancer: disease control and quality of life at 6 years. *Radiat Oncol* (2013) 8:118. doi: 10.1186/1748-717X-8-118
- Kishan AU, Dang A, Katz AJ, Mantz CA, Collins SP, Aghdam N, et al. Long-term Outcomes of Stereotactic Body Radiotherapy for Low-Risk and Intermediate-Risk Prostate Cancer. *JAMA Netw Open* (2019) 2(2):e188006. doi: 10.1001/jamanetworkopen.2018.8006
- Jackson WC, Silva J, Hartman HE, Dess RT, Kishan AU, Beeler WH, et al. Stereotactic Body Radiation Therapy for Localized Prostate Cancer: A Systematic Review and Meta-Analysis of Over 6,000 Patients Treated On Prospective Studies. *Int J Radiat Oncol Biol Phys* (2019) 104(4):778–89. doi: 10.1016/j.ijrobp.2019.06.1912
- Mahase SS, D'Angelo D, Kang J, Hu JC, Barbieri CE, Nagar H. Trends in the Use of Stereotactic Body Radiotherapy for Treatment of Prostate Cancer in the United States. *JAMA Netw Open* (2020) 3(2):e1920471. doi: 10.1001/jamanetworkopen.2019.20471
- Halpern JA, Sedrakyan A, Hsu WC, Mao J, Daskivich TJ, Nguyen PL, et al. Use, complications, and costs of stereotactic body radiotherapy for localized prostate cancer. *Cancer* (2016) 122(16):2496–504. doi: 10.1002/cncr.30101
- Baker BR, Basak R, Mohiuddin JJ, Chen RC. Use of stereotactic body radiotherapy for prostate cancer in the United States from 2004 through 2012. *Cancer* (2016) 122(14):2234–41. doi: 10.1002/cncr.30034
- Mahal BA, Chen YW, Sethi RV, Padilla OA, Yang DD, Chavez J, et al. Travel distance and stereotactic body radiotherapy for localized prostate cancer. *Cancer* (2018) 124(6):1141–9. doi: 10.1002/cncr.31190
- Levin-Epstein R, Cook RR, Wong JK, Stock RG, Jeffrey Demanes D, Collins SP, et al. Prostate-specific antigen kinetics and biochemical control following stereotactic body radiation therapy, high dose rate brachytherapy, and low dose rate brachytherapy: A multi-institutional analysis of 3502 patients. *Radiation Oncol* (2020) 151:26–32. doi: 10.1016/j.radonc.2020.07.014
- Kotecha R, Djemil T, Tendulkar RD, Reddy CA, Thousand RA, Vassil A, et al. Dose-Escalated Stereotactic Body Radiation Therapy for Patients With Intermediate- and High-Risk Prostate Cancer: Initial Dosimetry Analysis and Patient Outcomes. *Int J Radiat Oncol Biol Phys* (2016) 95(3):960–4. doi: 10.1016/j.ijrobp.2016.02.009
- Murthy V, Gupta M, Mulye G, Maulik S, Munshi M, Krishnatry R, et al. Early Results of Extreme Hypofractionation Using Stereotactic Body Radiation Therapy for High-risk, Very High-risk and Node-positive Prostate Cancer. *Clin Oncol (R Coll Radiol)* (2018) 30(7):442–7. doi: 10.1016/j.clon.2018.03.004
- Gonzalez-Motta A, Roach M3. Stereotactic body radiation therapy (SBRT) for high-risk prostate cancer: Where are we now? *Pract Radiat Oncol* (2018) 8(3):185–202. doi: 10.1016/j.prro.2017.11.008
- National Comprehensive Cancer Network. *Prostate Cancer (Version 2.2020)*. Available at: [http://www.nccn.org/professionals/physician\\_gls/pdf/prostate.pdf](http://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf) (Accessed July 28, 2020).
- Widmark A, Gunnlaugsson A, Beckman L, Thellenberg-Karlsson C, Hoyer M, Lagerlund M, et al. Ultra-hypofractionated versus conventionally fractionated radiotherapy for prostate cancer: 5-year outcomes of the HYPO-RT-PC randomised, non-inferiority, phase 3 trial. *Lancet* (2019) 394(10196):385–95. doi: 10.1016/S0140-6736(19)31131-6

29. Anwar M, Weinberg V, Chang AJ, Hsu IC, Roach M3, Gottschalk A. Hypofractionated SBRT versus conventionally fractionated EBRT for prostate cancer: comparison of PSA slope and nadir. *Radiat Oncol* (2014) 9:42. doi: 10.1186/1748-717X-9-42
30. Kishan AU, Wang PC, Upadhyaya SK, Hauswald H, Demanes DJ, Nickols NG, et al. SBRT and HDR brachytherapy produce lower PSA nadirs and different PSA decay patterns than conventionally fractionated IMRT in patients with low- or intermediate-risk prostate cancer. *Pract Radiat Oncol* (2016) 6(4):268–75. doi: 10.1016/j.prro.2015.11.002
31. Hegde JV, Collins SP, Fuller DB, King CR, Demanes DJ, Wang PC, et al. A Pooled Analysis of Biochemical Failure in Intermediate-risk Prostate Cancer Following Definitive Stereotactic Body Radiotherapy (SBRT) or High-Dose-Rate Brachytherapy (HDR-B) Monotherapy. *Am J Clin Oncol* (2018) 41(5):502–7. doi: 10.1097/COC.0000000000000311
32. Alayed Y, Cheung P, Pang G, Mamedov A, D'Alimonte L, Deabreu A, et al. Dose escalation for prostate stereotactic ablative radiotherapy (SABR): Late outcomes from two prospective clinical trials. *Radiother Oncol* (2018) 127(2):213–8. doi: 10.1016/j.radonc.2018.03.005
33. Levin-Epstein RG, Jiang NY, Wang X, Upadhyaya SK, Collins SP, Suy S, et al. Dose-response with stereotactic body radiotherapy for prostate cancer: A multi-institutional analysis of prostate-specific antigen kinetics and biochemical control. *Radiother Oncol* (2020) 154:207–13. doi: 10.1016/j.radonc.2020.09.053
34. Fuller DB, Falchhook AD, Crabtree T, Kane BL, Medbery CA, Underhill K, et al. Phase 2 Multicenter Trial of Heterogeneous-dosing Stereotactic Body Radiotherapy for Low- and Intermediate-risk Prostate Cancer: 5-year Outcomes. *Eur Urol Oncol* (2018) 1(6):540–7. doi: 10.1016/j.euo.2018.06.013
35. Yu JB, Cramer LD, Herrin J, Soulos PR, Potosky AL, Gross CP. Stereotactic body radiation therapy versus intensity-modulated radiation therapy for prostate cancer: comparison of toxicity. *J Clin Oncol* (2014) 32(12):1195–201. doi: 10.1200/JCO.2013.53.8652
36. Evans JR, Zhao S, Daignault S, Sanda MG, Michalski J, Sandler HM, et al. Patient-reported quality of life after stereotactic body radiotherapy (SBRT), intensity modulated radiotherapy (IMRT), and brachytherapy. *Radiother Oncol* (2015) 116(2):179–84. doi: 10.1016/j.radonc.2015.07.016
37. Meier R. Dose-Escalated Robotic SBRT for Stage I-II Prostate Cancer. *Front Oncol* (2015) 5:48. doi: 10.3389/fonc.2015.00048
38. Vargas CE, Schmidt MQ, Niska JR, Hartsell WF, Keole SR, Doh L, et al. Initial toxicity, quality-of-life outcomes, and dosimetric impact in a randomized phase 3 trial of hypofractionated versus standard fractionated proton therapy for low-risk prostate cancer. *Adv Radiat Oncol* (2018) 3(3):322–30. doi: 10.1016/j.adro.2018.02.004
39. Brand DH, Tree AC, Ostler P, van der Voet H, Loblaw A, Chu W, et al. Intensity-modulated fractionated radiotherapy versus stereotactic body radiotherapy for prostate cancer (PACE-B): acute toxicity findings from an international, randomised, open-label, phase 3, non-inferiority trial. *Lancet Oncol* (2019) 20(11):1531–43. doi: 10.1016/S1470-2045(19)30569-8
40. Prada PJ, Anchueto J, Blanco AG, Paya G, Cardenal J, Acuna E, et al. Low-dose-rate brachytherapy for patients with transurethral resection before implantation in prostate cancer. Longterm results. *Int Braz J Urol* (2016) 42(1):47–52. doi: 10.1590/S1677-5538.IBJU.2014.0531
41. Stone NN, Ratnow ER, Stock RG. Prior transurethral resection does not increase morbidity following real-time ultrasound-guided prostate seed implantation. *Tech Urol* (2000) 6(2):123–7.
42. Salembier C, Henry A, Pieters BR, Hoskin P. A history of transurethral resection of the prostate should not be a contra-indication for low-dose-rate 125I prostate brachytherapy: results of a prospective Uro-GEC phase-II trial. *J Contemp Brachyther* (2020) 12(1):1–5. doi: 10.5114/jcb.2020.92913
43. Eade TN, Horwitz EM, Ruth K, Buyyounouski MK, D'Ambrosio DJ, Feigenberg SJ, et al. A comparison of acute and chronic toxicity for men with low-risk prostate cancer treated with intensity-modulated radiation therapy or (125I) permanent implant. *Int J Radiat Oncol Biol Phys* (2008) 71(2):338–45. doi: 10.1016/j.ijrobp.2007.10.019
44. Wang K, Chen RC, Kane BL, Medbery CA, Underhill KJ, Gray JR, et al. Patient and Dosimetric Predictors of Genitourinary and Bowel Quality of Life After Prostate SBRT: Secondary Analysis of a Multi-institutional Trial. *Int J Radiat Oncol Biol Phys* (2018) 102(5):1430–7. doi: 10.1016/j.ijrobp.2018.06.066
45. Murthy V, Sinha S, Kannan S, Datta D, Das R, Bakshi G, et al. Safety of Prostate Stereotactic Body Radiation Therapy after Transurethral Resection of Prostate (TURP): A Propensity Score Matched Pair Analysis. *Pract Radiat Oncol* (2019) 9(5):347–53. doi: 10.1016/j.prro.2019.04.003
46. Xie Y, Djajaputra D, King CR, Hossain S, Ma L, Xing L. Intrafractional motion of the prostate during hypofractionated radiotherapy. *Int J Radiat Oncol Biol Phys* (2008) 72(1):236–46. doi: 10.1016/j.ijrobp.2008.04.051
47. van de Water S, Valli L, Aluwini S, Lanconelli N, Heijmen B, Hoogeman M. Intrafraction prostate translations and rotations during hypofractionated robotic radiation surgery: dosimetric impact of correction strategies and margins. *Int J Radiat Oncol Biol Phys* (2014) Apr 188(5):1154–60. doi: 10.1016/j.ijrobp.2013.12.045
48. Amro H, Hamstra DA, Mcshan DL, Sandler H, Vineberg K, Hadley S, et al. The dosimetric impact of prostate rotations during electromagnetically guided external-beam radiation therapy. *Int J Radiat Oncol Biol Phys* (2013) 85(1):230–6. doi: 10.1016/j.ijrobp.2012.03.020
49. Lovelock DM, Messineo AP, Cox BW, Kollmeier MA, Zelefsky MJ. Continuous monitoring and intrafraction target position correction during treatment improves target coverage for patients undergoing SBRT prostate therapy. *Int J Radiat Oncol Biol Phys* (2015) 91(3):588–94. doi: 10.1016/j.ijrobp.2014.10.049
50. Jackson WC, Dess RT, Litzenberg DW, Li P, Schipper M, Rosenthal SA, et al. A multi-institutional phase 2 trial of prostate stereotactic body radiation therapy (SBRT) using continuous real-time evaluation of prostate motion with patient-reported quality of life. *Pract Radiat Oncol* (2018) 8(1):40–7. doi: 10.1016/j.prro.2017.08.004
51. Gomez CL, Xu X, Qi XS, Wang PC, Kupelian P, Steinberg M, et al. Dosimetric parameters predict short-term quality-of-life outcomes for patients receiving stereotactic body radiation therapy for prostate cancer. *Pract Radiat Oncol* (2015) 5(4):257–62. doi: 10.1016/j.prro.2015.01.006
52. Culp SH, Schellhammer PF, Williams MB. Might men diagnosed with metastatic prostate cancer benefit from definitive treatment of the primary tumor? A SEER-based study. *Eur Urol* (2014) 65(6):1058–66. doi: 10.1016/j.eururo.2013.11.012
53. Rusthoven CG, Jones BL, Flaig TW, Crawford ED, Koshy M, Sher DJ, et al. Improved Survival With Prostate Radiation in Addition to Androgen Deprivation Therapy for Men With Newly Diagnosed Metastatic Prostate Cancer. *J Clin Oncol* (2016) 34(24):2835–42. doi: 10.1200/JCO.2016.67.4788
54. Weckermann D, Polzer B, Ragg T, Blana A, Schlimok G, Arnholdt H, et al. Perioperative activation of disseminated tumor cells in bone marrow of patients with prostate cancer. *J Clin Oncol* (2009) 27(10):1549–56. doi: 10.1200/JCO.2008.17.0563
55. Tzelepi V, Efsthathiou E, Wen S, Troncoso P, Karlou M, Pettaway CA, et al. Persistent, biologically meaningful prostate cancer after 1 year of androgen ablation and docetaxel treatment. *J Clin Oncol* (2011) 29(18):2574–81. doi: 10.1200/JCO.2010.33.2999
56. Parker CC, James ND, Brawley CD, Clarke NW, Hoyle AP, Ali A, et al. Systemic Therapy for Advanced or Metastatic Prostate Cancer: Evaluation of Drug Efficacy (STAMPEDE) investigators. Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial. *Lancet* (2018) 392(10162):2353–66. doi: 10.1016/S0140-6736(18)32486-3
57. Burdett S, Boevé LM, Ingleby FC, Fisher DJ, Rydzewska LH, Vale CL, et al. STOPCAP M1 Radiotherapy Collaborators. Prostate Radiotherapy for Metastatic Hormone-sensitive Prostate Cancer: A STOPCAP Systematic Review and Meta-analysis. *Eur Urol* (2019) 76(1):115–24. doi: 10.1016/j.eururo.2019.02.003
58. Palma DA, Olson R, Harrow S, Gaede S, Louie AV, Haasbeek C, et al. Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial. *Lancet* (2019) 393(10185):2051–8. doi: 10.1016/S0140-6736(18)32487-5

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