Clinical and Translational Radiation Oncology 50 (2025) 100888

Contents lists available at ScienceDirect

Clinical and Translational Radiation Oncology

journal homepage: www.sciencedirect.com/journal/clinical-and-translational-radiation-oncology

# Elective pelvic nodal irradiation in elderly men treated with hypofractionated radiotherapy

We thank Professor Iori and colleagues for their thoughtful commentary on our analysis of ultrahypofractionated (UHRT) versus moderately hypofractionated (MHRT) versus conventionally fractionated radiotherapy (CFRT) to the prostate in the setting of elective pelvic nodal irradiation (EPNI) for men with unfavourable prostate cancer [1]. The patients included were largely ≥70 years old [1]. With almost 6 years of follow-up, there were no differences in oncologic outcomes between the groups [1].

We observed increased late grade ≥ 2 and ≥ 3 gastrointestinal (GI) toxicity for patients treated with MHRT, where age was significantly associated with higher risk of late grade ≥ 2 GI toxicity [1]. It remains unclear why MHRT was associated with worse late GI toxicity and why there was an association with age; importantly, this was not seen in the UHRT group. Reassuringly, other phase 3 randomized studies of MHRT versus CFRT including PCS5 [2] and POP-RT [3,4] did not demonstrate worsening late GI toxicity and no age association with toxicity, providing further reassurance of the safety of MHRT, including in elderly patients. Further efforts to reduce dose to the rectum through rectal spacers, which were not utilized in these studies, is also a consideration for patients.

We also demonstrated that UHRT was associated with worse acute grade ≥ 2 genitourinary (GU) toxicity, with no association with patient age, and no worse acute grade ≥ 3 GU toxicity [1]. This toxicity seemed to be transient, as there was no worsening of late GU toxicities [1]. Further reassuringly, an interim analysis from the PRIME trial (NCT03561961) of UHRT versus MHRT EPNI did not show differences in acute grade ≥ 2 GU toxicity [5].

While UHRT and MHRT appear safe when delivering EPNI, our study did not address the role of EPNI compared to prostate-only RT, which Iori et al address. To date, the data supporting EPNI (irrespective of fractionation) remains controversial with negative older trials including GETUG-1 [6,7] and RTOG-9413 [8,9]. We continue to await the results from RTOG-0924 (NCT01368588) which has completed accrual. Currently, the most relevant contemporary study testing EPNI versus prostate only RT is the POP-RT trial, which demonstrated significant improvement with EPNI, both for 5-year biochemical failure free survival (95 % with EPNI versus 81.2 % with prostate-only RT; HR 0.23), and 5-year distant metastasis-free survival (95.9 % with EPNI versus 89.2 % with prostate-only RT; HR 0.35) [4]. Based on POP-RT, patients who do not receive EPNI may be up to approximately 4 times more likely to need androgen deprivation therapy (ADT) to manage biochemical failure and/or distant metastasis, with its own side effect profile and impact on long-term prognosis.

Ultimately, we support recommendations for the use of EPNI for patients at high risk of harboring nodal disease. However, assessment of individual patients including their values, medical comorbidities, and estimates of personal risks of toxicities should guide well-informed discussions to determine a person-centred treatment plan.

**Disclosures:**

RMG reports honoraria from Bayer, Tolmar, Knight, and TerSera; Research funding from Astellas and TerSera.

AL reports honoraria/travel from AbbVie, Astellas, Bayer, Janssen, Knight, TerSera; Grant/research support from TerSera and Tolmar; Advisory boards/consulting for Astellas, Bayer, Janssen, Sanofi, Tolmar and TerSera; Patents/licenses for endorectal immobilization device (GU-Lok); Employment: spouse is national sales director, Sanofi Canada.

PC reports honoraria from TerSera and AstraZeneca.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## References

[1] Glicksman RM, Loblaw A, Morton G, et al. Elective pelvic nodal irradiation in the setting of ultrahypofractionated versus moderately hypofractionated and conventionally fractionated radiotherapy for prostate cancer: outcomes from 3 prospective clinical trials. *Clin Transl Radiat Oncol* 2024;49:100843.

[2] Niazi T, Nabid A, Malagon T, et al. Hypofractionated, dose escalation radiation therapy for high-risk prostate cancer: the safety analysis of the prostate cancer study-5, a groupe de radio-oncologie Génito-Urinaire de Quebec led PHASE 3 trial. *Int J Radiat Oncol Biol Phys* 2024;118(1):52–62.

[3] Murthy V, Maitre P, Bhatia J, et al. Late toxicity and quality of life with prostate only or whole pelvic radiation therapy in high risk prostate cancer (POP-RT): a randomised trial. *Radiother Oncol* 2020;145:71–80.

[4] Murthy V, Maitre P, Kannan S, et al. Prostate-only versus whole-pelvic radiation therapy in high-risk and very high-risk prostate cancer (POP-RT): outcomes from phase III randomized controlled trial. *J Clin Oncol* 2021;39(11):1234–42.

[5] Murthy V, Maitre P, Arunsingh M, et al. OC-0924 prostate RT In high risk or N+ moderate vs extreme hypofractionation (PRIME): an interim analysis. *Radiother Oncol* 2023;182:S770–1.

[6] Pommier P, Chabaud S, Lagrange JL, et al. Is there a role for pelvic irradiation in localized prostate adenocarcinoma? Preliminary results of GETUG-01. *J Clin Oncol* 2007;25(34):5366–73.

[7] Pommier P, Chabaud S, Lagrange JL, et al. Is there a role for pelvic irradiation in localized prostate adenocarcinoma? update of the long-term survival results of the GETUG-01 randomized study. Int J Radiat Oncol Biol Phys 2016;96(4):759–69.

[8] Roach 3rd M, DeSilvio M, Lawton C, et al. Phase III trial comparing whole-pelvic versus prostate-only radiotherapy and neoadjuvant versus adjuvant combined androgen suppression: radiation therapy oncology group 9413. *J Clin Oncol* 2003;21(10):1904–11.

[9] Roach M, Moughan J, Lawton CAF, et al. Sequence of hormonal therapy and radiotherapy field size in unfavourable, localised prostate cancer (NRG/RTOG 9413): long-term results of a randomised, phase 3 trial. *Lancet Oncol* 2018;19(11):1504–15.

Rachel M. Glicksman[a], Andrew Loblaw[b,c,d], Patrick Cheung[b,c,*]

[a] *Radiation Medicine Program, Princess Margaret Cancer Centre, University Health Network, Toronto, Canada*

https://doi.org/10.1016/j.ctro.2024.100888

Received 25 October 2024; Accepted 12 November 2024

Available online 14 November 2024

[b] *Department of Radiation Oncology, Odette Cancer Centre, Sunnybrook Health Sciences Centre, Toronto, Canada*
[c] *Department of Radiation Oncology, University of Toronto, Toronto, Canada*
[d] *Institute of Health Policy, Management and Evaluation, University of Toronto, Canada*

[*] Corresponding author.
*E-mail address:* patrick.cheung@sunnybrook.ca (P. Cheung).