



## Platinum Priority – Editorial

Referring to the article published on pp. 910–917 of this issue

# Balancing Risks in Prostate-specific Antigen Recurrence: The Fox Versus the Hedgehog

Bridget F. Koontz\*

Department of Radiation Oncology, Duke Cancer Institute, Durham, NC, USA

There are clear dichotomies in prostate cancer—men aged in their 90s who have been living with prostate cancer for 20 years, and 55-year-old men who die within 3 years of diagnosis. But much more heavily populated than these extremes is the space between—where it is difficult to predict who will do well with minimal intervention and who will progress, allowing an opportunity for early intervention to change disease trajectory. Since we are unlikely to accurately predict every patient's outcome, how do we balance the risks and benefits of overtreatment with those of undertreatment?

One outstanding controversy in the management of prostate cancer regards the role of adjuvant and salvage radiotherapy after prostatectomy. Three randomized trials show improvement in biochemical control with early postoperative radiotherapy, one also showing an overall survival advantage [1–3]. However, these studies have their criticisms and ultimately, clinical practice has favored ultrasensitive prostate-specific antigens (PSAs) and delivery of early salvage for many patients. Prospective clinical trials are pending, but large retrospective studies suggest that generally postoperative radiotherapy is more effective at lower PSAs [4], although low-risk cancers may be suitable for a surveillance approach.

In this month's issue of *European Urology*, Dr. Gandaglia and colleagues [5] describe a new nomogram meant to provide insight into the likelihood of prostate cancer death in men with a persistently detectable PSA after radical prostatectomy. This study provides additional evidence that postoperative radiotherapy can reduce the likelihood of prostate cancer death in men with highly aggressive prostate cancer. The authors also note that some patients had a low risk of prostate cancer death and could be

managed expectantly without immediate salvage treatment.

While at first this report seems concerning in a relegation of radiotherapy to a minority of men, with some consideration I view it overall to be useful data when taken in context. The specific question posed by the authors is whether immediate radiotherapy for detectable PSAs is necessary in all men. It is probable that many of the patients in the “no radiotherapy” group eventually did receive salvage treatment. In that case, this describes outcomes of early versus late salvage. The data supports that in men with low-risk disease, early treatment may not be necessary and PSA can be safely monitored, initiating treatment when PSA begins to rise—active surveillance in the postoperative setting. One possibility is that delayed radiotherapy is still effective at curing the cancer and remission is achieved, but the delay maximizes urinary and sexual recovery. Another is that these cancers are instead being managed long term by salvage androgen deprivation. However, this latter explanation carries another concern, which is that an endpoint of mortality may be missing significant negative quality of life factors if patients achieve freedom from prostate cancer death by many years of hypogonadism.

Philosophers apply the quote “the fox knows many things, but the hedgehog knows one big thing” by Greek poet Archilochus to illustrate the different ways humans think; for some all experiences can be seen through the lens of one grand vision, and others for whom life cannot be simplified to fit into one truth. Both have advantages and disadvantages. But in prediction, the fox has an advantage as it is more flexible and adaptable to new data and alternate explanations [6]. As we improve our science to provide more individualized medicine, we must be careful not to oversimplify and put

DOI of original article: <http://dx.doi.org/10.1016/j.eururo.2017.06.001>.

\* Department of Radiation Oncology, Duke Cancer Institute, Durham, NC 27710, USA. Tel. +1 919 668 5213; Fax: +1 919 668 7345.

E-mail address: [bridget.koontz@duke.edu](mailto:bridget.koontz@duke.edu).

<http://dx.doi.org/10.1016/j.eururo.2017.07.021>

0302-2838/© 2017 European Association of Urology. Published by Elsevier B.V. All rights reserved.



every patient into the same basket. One risk with the presented nomogram is that it includes androgen deprivation therapy use as a factor—a subjective measure which is a surrogate for other disease factors not measured in the nomogram. Postoperative PSA velocity is not taken into account. These patients come from a long-time period, much of which was a different era in terms of the clinical risk groups of patients undergoing prostatectomy. The study offers valuable insight that not all men with a residual PSA after prostatectomy require immediate additional treatment, but they still require complex consideration of many variables in making a recommendation for or against salvage radiotherapy.

**Conflicts of interest:** Koontz receives unrestricted research funding from Janssen Pharmaceuticals, and is an advisory board member for Blue Earth Diagnostics.

## References

- [1] Bolla M, van Poppel H, Tombal B, et al. Postoperative radiotherapy after radical prostatectomy for high-risk prostate cancer: long-term results of a randomised controlled trial (EORTC trial 22911). *Lancet* 2012;380:2018–27.
- [2] Thompson IM, Tangen CM, Paradelo J, et al. Adjuvant radiotherapy for pathological T3N0M0 prostate cancer significantly reduces risk of metastases and improves survival: long-term followup of a randomized clinical trial. *J Urol* 2009;181:956–62.
- [3] Wiegel T, Bartkowiak D, Bottke D, et al. Adjuvant radiotherapy versus wait-and-see after radical prostatectomy: 10-year follow-up of the ARO 96-02/AUO AP 09/95 trial. *Eur Urol* 2014;66:243–50.
- [4] Tendulkar RD, Agrawal S, Gao T, et al. Contemporary update of a multi-institutional predictive nomogram for salvage radiotherapy after radical prostatectomy. *J Clin Oncol* 2016;34:3648–54.
- [5] Gandaglia G, Boorjian SA, Parker WP, et al. Impact of postoperative radiotherapy in men with persistently elevated prostate-specific antigen after radical prostatectomy for prostate cancer: a long-term survival analysis. *Eur Urol* 2017;72:910–7.
- [6] Tetlock PE. *Expert political judgment: how good is it? How can we know?*. Princeton, NJ: Princeton University Press; 2005.



Apply for your EAU membership online!

Would you like to receive all the benefits of EAU membership, but have no time for tedious paperwork?

**Becoming a member is now fast and easy!**

Go to [uroweb.org/membership](http://uroweb.org/membership) to apply online. It will only take you a couple of minutes to submit your application, the rest is for you to enjoy!