Toxicity of Stereotactic Body Radiation Therapy Versus Intensity-Modulated Radiation Therapy for Prostate Cancer: A Potential Comparison Bias

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To the Editor: In their recent article, Yu et al compared the toxicity and cost effectiveness of two radical forms of radiotherapy (stereotactic body radiation therapy [SBRT] *v* intensity-modulated radiation therapy [IMRT]) for the treatment of prostate cancer (PCa). Their retrospective analysis, performed by using a random effects model to compare toxicities between matched patients who received SBRT or IMRT as primary treatment from 2008 and 2011, concluded that SBRT is associated with increased rate of genito-urinary (GU) toxicity despite lower treatment costs. We appreciated that the authors themselves recognized the several limitations of the study, some of which were partly addressed in the Discussion. Nevertheless, there is no doubt that the message brought to the oncological community via a highly accessed journal sounds like a serious warning against a potential harmfulness of SBRT, but it is likely to be misleading. We are aware that long follow-up and accurate evaluation of GU toxicity are important, as the urethra is unavoidably at risk in irradiation of the prostate, and there are some uncertainties in extrapolating biologic effects to large fraction size. However, these concerns should be investigated in appropriate randomized trials, or at least in thoroughly assessed retrospective analyses. In our opinion, relevant pitfalls affect the findings of this article. First, the authors did not report the scale and the grade of the toxicity. This represents a crucial bias because the same signs or symptoms might be scored differently according to the system that has been adopted (ie, acute urinary retention is classified as grade 3 and grade 2 toxicity according to the Radiation Therapy Oncology Group[1] and Common Terminology Criteria for Adverse Events version 4.0,[2] respectively), and their clinical relevance is important in the evaluation of an innovative therapeutic approach. Second, it appears that they used the same scoring to account for both early (< 6 months) and late (≥ 6 months) toxicity. This makes it rather unclear which GU toxicity they are really dealing with. Moreover, some diagnostic procedures were considered as a surrogate for treatment-related adverse events: this represents a subjective criterion and should not be used as a reliable argument to evaluate toxicity outcomes. Furthermore, the authors claimed that some unknown confounders would have likely biased the results in favor of SBRT, because in the timeframe of the study it was adopted for low-risk disease, whereas IMRT would have likely been used for extended-field pelvic irradiation in higher risk disease. This statement indeed reflects a personal point of view that runs counter to evidence[3] showing that GU symptoms during and after the radiation course might increase in low-risk patients (SBRT group) who do not benefit from the cytoreductive effect of the hormonal manipulation like high-risk patients (IMRT group) did. Finally, radiotherapy-related toxicities are highly dependent on the radiation dose, fields used, and dose-volume constraints. The lack of these data makes any considerations about toxicity rather speculative. In conclusion, we believe that such a biased analysis cannot draw any definitive conclusion regarding increased toxicity of SBRT compared with IMRT. SBRT has been shown to be a promising tool to treat various types of primary and metastatic solid tumors[4,5] and in prostate cancer has shown better conformality than IMRT,[6] as well as excellent outcomes in terms of both toxicity and local control.[7] Although its efficacy needs to be fully validated with long-term follow-up, it is undeniable that for the intrinsic radiobiologic characteristics of PCa, along with economical and logistic convenience, SBRT should be considered an alternative to conventionally fractionated regimens in the management of localized PCa, provided that appropriate technology, physics, and clinical expertise are present. This could necessitate a major educational effort for the oncological community caring for patients with PCa.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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