Highlight of Papers

Brachytherapy boost improves survival and decreases the risk of developing distant metastases compared to external beam radiotherapy alone in intermediate and high-risk group prostate cancer patients.

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What was your motivation for initiating this study?

Prostate cancer (PCa) is a significant contributor to cancer incidence and mortality rates worldwide. While the combination of brachytherapy boost (BTB) and external beam radiotherapy (EBRT) has brought improved biochemical control in intermediate- and high-risk PCa patients compared with the use of EBRT alone, the existing prospective randomised studies (1-3) have not demonstrated significant improvements in overall survival (OS) or time to (freedom from) distant metastases (FFDM). However, even the largest available trial (ASCENDE-RT), which compared low-dose-rate BTB with dose-escalated EBRT, was never powered to test for differences in such endpoints (4). While improving the period to prostate-specific antigen failure does indicate clinical benefit, it was deemed insufficient as a surrogate for survival in PCa trials in a recent meta-analysis (5), prompting us to initiate this project.

The earlier clinical trials were rather modest in terms of the size of study groups and utilised radiotherapy and androgen-deprivation therapy schedules that could be considered insufficient according to the current standards of care (1-2). Therefore, instead of a meta-analysis, we decided to reach out for real-world data to analyse a significantly larger, modern dataset. The main intent of this study was to assess the association between BTB, survival outcomes, and the risk of distant metastases in intermediate- and high-risk PCa patients to see whether BTB improved clinically relevant outcomes in real-world settings.

What were the main challenges during the work?

Considering the retrospective character of our analysis, there were several challenges to be met. We planned to match propensity scores for clinical prognostic factors, multivariable models, and several subset analyses to account for selection bias. However, we also had to consider non-obvious confounders (e.g., significant differences in life expectancy for given populations), while simultaneously gathering enough data to overcome the limitations of previously described trials. Since BTB is not as widely used as EBRT, it was a challenge to set up multi-institutional collaboration, but we were able to collect data on 1641 patients who had been treated with high-dose-rate BTB or EBRT between 2003 and 2014. This is over fourfold larger study group compared to the ASCENDE-RT trial.

What are the most important findings of your study?

We found that dose escalation with BTB was associated with clinically relevant improvements in OS, FFDM, and metastases-free survival in real-world settings. These results were consistent both in propensity-score matching analysis, the multivariable regression model, and subset analyses for relevant risk groups. Our study confirms the clinical benefit of BTB that has been indicated by improved biochemical control in prospective randomised trials (1-3).

What are the implications of this research?

Despite low accessibility and a complicated treatment procedure, BTB is an excellent way to improve outcomes in patients with clinically relevant localised PCa. The dose conformity is unmatched and several aspects are difficult to mimic with non-invasive modalities, such as the immune effect associated with hotspots around catheters. It is possible that the full potential of BTB is still

underestimated, and prospective trials are highly warranted, especially those that combine the use of prostate-specific membrane antigen/positron emission tomography (PSMA-PET) medical imaging with systemic treatment escalation in high-risk PCa patients. For now, we believe that BTB is a valuable treatment modality and that patients should be informed about the possibility and associated pros and cons of combining EBRT with BTB to treat those with intermediate- or high-risk PCa.

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