Long-term outcomes of ultra-hypofractionated 2 fractions single day HDR brachytherapy in localised prostate cancer

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What was your motivation for initiating this work?

The main treatment options for clinically localised prostate cancer, which are radical prostatectomy, external beam radiotherapy (EBRT) and brachytherapy (BT), are considered to have comparable efficacy. As no consensus has been reached regarding the most appropriate treatment option, factors such as impact on quality of life, duration of treatment, convenience and cost-effectiveness all play important roles in the treatment choice.

High-dose-rate BT (HDR-BT) has been utilised to treat prostate cancer since the mid-1980s. In the mid-1990s, HDR-BT was proposed as a monotherapy for localised prostate cancer, and since then, numerous studies have demonstrated its safety and effectiveness through well-established outcomes.

In cases in which the alpha/beta-ratio of the prostate cancer is considered low, ultra-hypofractionated treatments could be advantageous in terms of radiation biology and therefore, their use could increase the therapeutic ratio. HDR-BT has been studied extensively in these terms, although low-dose-rate BT (LDR-BT) has been studied more and has become a standard treatment option because its use offers good clinical local control rates. The use of HDR-BT has been associated with decreased rates of acute and chronic urinary frequency, urgency, dysuria, rectal pain and grade-2 rectal toxicity compared with LDR-BT. However, a dramatic decrease was also noted in the rate of sexual function in patients who had undergone HDR-BT.

Given the potential advantages of treatment with HDR-BT, and in an attempt to make prostate HDR-BT more attractive and efficient, in 2010 we conducted a prospective study of single-implant HDR-BT delivered as two fractions, each of 13.5Gy, within one day. We hypothesised that this prescription would be well tolerated and effective. Our primary objective was to evaluate the acute and late toxicities that were caused through the use of this treatment protocol and the biochemical and clinical disease control rates that were achieved. The secondary objective was to explore long-term outcomes and to investigate the relationship between the lowest levels of prostate-specific antigen (PSA nadir) that were recorded and biochemical control.

What were the main challenges of this work?

The idea for this study originated during a clinical trial of the application of two fractions of HDR-BT in one day to treat localised prostate cancer. The trial was performed in the William Beaumont Hospital by Dr A. Martinez and Dr Ghilezan. The challenge in their study was to improve the comfort of the patient and to reduce the cost of the procedure.

Therefore, we designed a brachytherapy table-bed to be used for the entire procedure (including insertion of catheters, transfer to the planning CT, treatment and the waiting period between the two sessions) and an abdominal belt with two elastic perineal bands that would support the template. The first 50 patients underwent two CT scans: the first after the implant, in order to aid dosimetry planning, and the second before the administration of the second HDR-BT fraction, in order to check for possible displacements. We did not find needle displacements ≥5mm so the immobilisation system was approved, and we were considered unnecessary for further cases.
To ensure that the patients were kept comfortable with sufficient pain control throughout the process, epidural anaesthesia was employed.

What are the most important outcomes of this work?

The median follow-up of the cohort was 123 months. This study showed the results after a long-term follow-up of our 2018 report.
In our 2018 publication, we stated that the cumulative incidence of acute-grades 2 and 3 genitourinary (GU) toxicity was 9% and 2%, respectively. The corresponding incidences of late GU toxicity were 18% and 1%. Only one patient experienced late-grade 2 gastrointestinal toxicity. No toxicity of grades 4 or 5 was detected (1).
It was found that 13.3% of patients died without prostate cancer. The number of patients who showed post-treatment failure was very low; 6.7% of patients experienced biochemical failure and 3.3% presented with distant metastases. Ten-year actuarial rates of no biochemical evidence of disease (bNED), overall survival, local control and metastasis-free survival for all patients were 93.3%, 86.7%, 95.2% and 96.1%, respectively.
The median period to achieve PSA nadir was 80.5 months. Nearly three-quarters (74.2%) of patients who were alive showed undetectable PSA levels (≤0.20ngml^{-1}) after four years of follow-up. Moreover, 95.8% of living patients who showed no biochemical failure showed undetectable PSA levels (≤0.20ngml^{-1}) at the 10-year follow-up point.

Patients who attained a PSA nadir of ≤0.20ngml^{-1} exhibited a 10-year bNED survival rate of 96.9%, whereas those who failed to reach this PSA level had a survival rate of only 40%.

What are the implications of this research?

The results of our study demonstrate that ultra-hypofractionated HDR-BT at a dose of 27Gy delivered in two fractions on the same day controls the disease excellently with low toxicity and good cost efficiency.
In patients with favourable localised prostate cancer, two-fraction HDR-BT monotherapy is a highly curative radiation technique that attains PSA nadir levels of <0.2ngml^{-1} in 95% of cases.

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