Editors' pick

Ultra-hypofractionated radiotherapy for low- and intermediate-risk prostate cancer: high-dose-rate brachytherapy vs. stereotactic ablative radiotherapy

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What was your motivation for initiating this study?

There is increasing interest in the delivery of radiotherapy for prostate cancer (PCa) through use of stereotactic ablative body radiotherapy (SABR). Use of this technique enables delivery of high doses per fraction and therefore exploitation of the low α/β ratio of this tumour and its high sensitivity to the size of the radiation fraction. Ultra-hypofractionated high-dose-rate brachytherapy (HDR BT) as monotherapy is another means of delivering extreme hypofractionation. Two schedules have been used at Mount Vernon Cancer Centre (Middlesex, UK) in recent years: a 19Gy single dose or 26Gy in two fractions. We have also developed an SABR technique to deliver 36.25Gy in five fractions to patients with low- and intermediate risk PCa.

Against this background, this study was conducted to compare the treatment outcomes, including biochemical control rates (BCRs), late gastrointestinal (GI) and genitourinary (GU) toxicities, for patients who received single-dose HDR BT, two-fraction HDR BT or five-fraction SABR.

What were the main challenges during the work?

This study was undertaken as a retrospective service evaluation of patients with low- and intermediate-risk PCa who had been treated between August 2008 and December 2017 through application of those three treatment schedules at our institution. The relatively small sample size and short follow-up period were the obvious shortfalls of our study. Also, the three separate treatment cohorts were compared with no randomised treatment allocation, and there were demographic differences between the treatment groups. This made it difficult to carry out the study as one that involved propensity score matching.

What are the most important findings of your study?

A total of 185 patients who had low- and intermediate-risk PCa and who received 19Gy/one fraction by HDR BT (78), 26Gy/two fractions by HDR BT (64) or 36.25Gy/five fractions by SABR (43) were included in this study. The median follow-up was 60.1 months (range 7.1-133.7 months).

The BCRs were 95% at three years and 85% at five years for all patients. The five-year BCRs were 69% (19Gy/one fraction), 95% (26Gy/two fractions) and 92% (36.25Gy/five fractions). No statistically significant difference in BCRs was found between the two-fraction HDR BT and five-fraction SABR ($p=0.37$) treatment arms, but the BCR of the single-fraction group was significantly worse than those of the other two groups ($p<0.05$).

The cumulative incidence of ≥grade 2 GI toxicities of the 19Gy/one fraction, 26Gy/ two fractions and 36.25Gy/five fractions were 0%, 2% and 4% at five years. Incidence rates in those treated in the five-fraction SABR arm were significantly higher ($p<0.05$) than the incidence rates in those who were treated in either one- or two-fraction HDR BT; no statistically significant difference was observed between the two HDR BT groups ($p=0.15$). The cumulative incidence rates of ≥grade 2 GU events in the 19Gy/one fraction, 26Gy/ two fractions and 36.25Gy/five fractions groups were 30%, 5% and 6% at five years. No statistically significant difference was

found between the 26Gy/two fractions and 36.25Gy/five fractions (p=0.37) treatment arms, but incidence rates in the 26Gy/two fractions patients were significantly lower than those seen in patients who received single-dose 19Gy HDR BT (p<0.05).

What are the implications of this research?

This study has demonstrated that 26Gy/two fractions HDR BT provided equivalent BCRs with lower toxicity compared with 36.25Gy/five fractions SABR, and that both two-fraction HDR BT and five-fraction SABR achieved better BCRs than single-dose 19Gy HDR BT. The immediate conclusion is that findings of other research studies are confirmed: that 19Gy single dose HDR BT is not adequate for patients with intermediate-risk PCa. The two-fraction HDR BT schedule should be considered as a standard of care and an important comparator in future clinical trials that aim to evaluate ultra-hypofractionated radiotherapy regimes in localised PCa. This demands ongoing support and development of brachytherapy services, which in many health care systems are showing a decline in activity as less well established SABR techniques are preferred.

Thank you for inviting us to discuss this recent publication with the readers of the European SocieTy for Radiotherapy and Oncology brachytherapy corner.

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