Beyond conventional or hypofractionated high-dose intensity-modulated radiotherapy for prostate cancer (CHHiP)

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Learning points

The five-year efficacy and toxicity outcomes from the CHHiP and PROFIT demonstrated that moderate hypofractionation is non-inferior to conventional fractionation recommending 60 Gray (Gy) in 20 fractions (hypo-RT) as the new standard of care. The estimated $\alpha/\beta$ for prostate cancer is 1.8 Gy. For low and intermediate risk patients, Hypo-radiotherapy (RT) to the prostate only combined with a short course of subsequent androgen deprivation therapy (ADT) achieves effective local and biochemical control. Survival is dominated by non-cancer death events, which is related to age and comorbidity. For high risk localised prostate cancer, hypo-RT with long course ADT improves survival and biochemical control compared to ADT only. Survival is dominated by cancer related mortality. The risk of local recurrence correlates with higher tumour grade and bulkier tumour volume.

Biochemical failure rates could potentially be improved by more intensive systemic therapy. Other possibilities are: increasing the radiotherapy delivery by focal dose escalation, combinations of hypo-RT with brachytherapy or pelvic node treatment.

Results of the randomised FLAME trial and a number of cohort studies have shown similar toxicity profiles of focal dose escalation. Multi-parametric magnetic resonance imaging (MRI) or positron emission tomography-computed tomography (PET-CT) imaging Choline or prostate-specific membrane antigen (PSMA) are used to define boost volumes. Inter-observer variations have shown to be significant; training and agreed guidelines are required. Hypo-RT can be combined with focal dose escalation.

In clinically node-negative patients with high-risk localised prostate cancer, surgical series have demonstrated high rates of pathological positive nodes, but the RTOG 9413 and GETUG trial, which included mostly low and intermediate risk participants did not demonstrate a benefit of pelvic node irradiation. It is not clear whether high-risk patients derive more benefit. In cohort studies, hypo-RT has been combined with pelvic node radiotherapy.

Randomised trials of high dose rate (HDR) brachytherapy or seed brachytherapy (ASCENDE) combined with RT compared to external beam radiotherapy (EBRT) only, resulted in an improvement of relapse-free survival at five years for high risk patients. HDR offers the advantage of excellent conformity, rapid dose fall-off outside the target volume and the possibility for dose escalation with sparing of the normal tissues.
References


Hypoxia modification and other novel drug combinations

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Learning points

Studies using oxygen-sensitive electrodes, immunohistochemistry and oxygen-sensitive imaging methods have confirmed the presence of variable levels of hypoxia within prostate tumours.

Men with hypoxic tumours have a worse prognosis following radical radiotherapy than men with well-oxygenated prostate cancers.

It is possible to reverse tumour hypoxia in prostate cancer using the relatively simple technique of carbogen and nicotinamide administration during radiotherapy (the PROCON method).

The first phase II trial of hypoxia modification in prostate cancer has now been completed, demonstrating safety and negligible additional toxicity compared to standard radiotherapy.

Prospective phase III trials are needed to demonstrate superiority of PROCON compared to standard radiotherapy and additional research into other hypoxia modification techniques for prostate radiotherapy are also required.

References

