Editor's picks

MRI assisted focal boost integrated with HDR monotherapy study in low and intermediate risk prostate cancer (MARS): Results from a phase II clinical trial.

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What was your motivation for initiating this study?

Our group has a keen interest in improving outcomes and reducing the treatment burden for men with localised prostate cancer. We believe that high-dose-rate (HDR) brachytherapy as monotherapy might maximise those outcomes.

Our group had performed a randomised study of 19 Gy x 1 versus 13.5 Gy x 2 to the whole gland, but very few of those patients underwent MR-guided brachytherapy.1,2 We wanted to formally assess whether 19 Gy x 1 to the whole gland with a simultaneous boost to the dominant intraprostatic lesion (DIL) would be technically feasible, well tolerated and effective.

What were the main challenges during the work?

The main challenge was to develop a reproducible way to contour the DIL. Initially we used cognitive fusion, but then developed an in-house deformable registration system to work with our ultrasound-based HDR planning system (Oncentra).

What were the most important findings of your study?

The most important outcome was the poorer-than-expected biochemical control. Despite giving a median dose to 90% of the DIL of > 27 Gy, the treatment had failed for over 30% of the patients by 48 months of follow-up. This is similar to other groups' experiences (including our own) when patients were treated with 19 Gy x 1 to the whole gland (without MR-boost). For comparison the 13.5 Gy x 2 HDR arm showed a 3% failure at five years.

What are the implications of this research?

It's possible that the mechanism of cell kill when using large single fractions of radiation is different from treatment that uses lower doses per fraction. Kolesnick and colleagues have done some work which suggests that the ceramide-mediated cell kill predominates when doses per fraction are greater than 10Gy and that defects in the acid sphingomyelinase pathway3 in some patients might explain reduced cell kill and therefore worse biochemical outcomes. However, until we sort out which patients it is safe to give large single fractions, these should not be offered to patients with prostate cancer (either as HDR or as stereotactic ablative body radiotherapy).

References

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