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Clinical Perspective

Tumour-Targeted Treatment Intensification for Prostate Cancer Using Magnetic Resonance Imaging Guidance

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ABSTRACT

Introduction: Local control in prostate cancer may be improved with targeted dose escalation to regions with high tumour burden. Multiparametric magnetic resonance imaging (mpMRI) combined with MRI-guided biopsies may aid in defining tumour-dense regions before radiation therapy. Deformable registration techniques may be used to map these tumour regions onto the radiotherapy planning MRI. Radiation therapy delivery techniques such as volumetric modulated arc therapy and high-dose-rate brachytherapy may allow for highly conformal dose escalation, and when coupled with image-guided radiation delivery (ie, cone beam computed technology and fiducial markers), may allow high-precision dose-escalated treatment.

Methods: Eligible prostate cancer patients were enrolled on a prospective trial of tumour dose escalation. Two strategies were investigated: (1) an integrated boost to external beam radiation for a total tumour dose of 95 Gy in 38 fractions or (2) a focal high-dose-rate boost of 10 Gy before 76 Gy in 38 fractions external beam radiation. Patients underwent MRI-guided biopsy with fiducial marker placement before therapy. mpMRI was acquired and used in conjunction with a non-endorectal coil T2 MRI and computed technology simulation images to define the gross tumour volume via a deformable registration approach for intra-prostatic tumour dose escalation.

Results: A case example for each dose escalation strategy illustrates the tumour-targeted approach using MRI guidance.

Conclusions: Combining mpMRI sequences with a deformable registration approach may aid in more accurate and reproducible definition of tumour-dense regions. This novel process coupled with daily image guidance may allow high-precision dose-escalated tumour-targeted radiotherapy for prostate cancer.

RÉSUMÉ

Introduction : Le contrôle local dans le cancer de la prostate peut être amélioré par une augmentation ciblée de la dose dans les régions à forte charge tumorale. L'IRM multi-paramétrique MRI (mpMRI) combinée à des biopsies guidée par IRM peut aider à définir les régions à forte densité tumorale avant le début de la radiothérapie. Les techniques de registration déformable peuvent être utilisées pour cartographier ces régions tumorales sur l'IRM de planification de la radiothérapie. Les techniques d'administration de la radiothérapie, comme l'irradiation avec modulation d'intensité volumétrique par arcthérapie (VMAT) et la brachythérapie à dose élevée (HDR) peuvent permettre une augmentation de dose hautement conforme, et, en association avec la radiothérapie guidée par l'image (p. ex. CBCT et repères de référence) peuvent permettre un traitement à dose augmentée de grande précision.

Méthodologie : Les patients atteints d'un cancer de la prostate admissible étaient inscrits à un essai prospectif d'augmentation de la dose tumorale. Deux stratégies ont été examinées: une augmentation intégrée à la radiothérapie par faisceau conique (EBRT) pour une dose tumorale totale de 95 Gy en 38 fractions, ou une augmentation focale en HDR de 10 Gy avant d'atteindre 76 Gy en 38 fractions EBRT. Les patients ont subi une biopsie guidée par IRM avec positionnement des repères de référence avant la thérapie. La mpMRI a été acquise et utilisée par IRM T2 avec coil non-endorectal (ERC) et images de simulation TDM pour définir le volume tumoral brut (GTV) par une approche de registration déformable pour augmentation de la dose tumorale intra-prostatique.

Résultats : Un exemple pour chaque stratégie d'augmentation de la dose illustre l'approche ciblée sur la tumeur par guidage IRM.

Conclusion : La combinaison de séquences mpMRI et d'une approche de registration déformable pourrait aider à obtenir une définition plus précise et reproductible des régions à haute densité

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tumorale. Ce processus innovateur, couplé au guidage par des images quotidiennes, pourrait permettre la radiothérapie à augmentation de dose ciblée sur la tumeur d'une précision élevée pour le cancer de la prostate.

Keywords: Prostate; radiation therapy; MRI; image guidance

Introduction

Prostate cancer remains the leading male cancer in Canada, with 21,000 new cases reported in 2016 [1]. External beam radiation (EBRT) therapy constitutes one of the primary modalities for prostate cancer treatment. Although there have been improvements in treatment delivery techniques and reduction in treatment-related toxicities, local recurrence remains a problem in some prostate cancers [2]. Improvement in local control and increasing the therapeutic index of radiotherapy continue to be a pressing need in prostate cancer. Local recurrence predominantly occurs in tumour-dense regions within the prostate [3]. Previous research has indicated that dose escalation to the whole gland has improved outcomes for a subset of patients with local disease [4]. One strategy investigated at the Princess Margaret Cancer Centre is dose escalation with a tumour-targeted approach.

Dose escalation to the tumour alone may improve local control while sparing the surrounding normal tissue. One critical factor for success of such an approach is the accurate and reproducible identification of the gross tumour volume (GTV) within the prostate. This is evolving with increased availability of multiparametric magnetic resonance imaging (mpMRI). Combining the sensitivity and specificity of mpMRI with an accurate deformable registration technique may define such tumour-dense regions for radiation treatment.

Advanced radiation delivery techniques such as volumetric modulated arc therapy (VMAT) with online cone beam computed tomography daily image guidance using implanted fiducial markers (FM) reduce target position uncertainties enabling a tumour-targeted approach for patients treated with EBRT alone. High-dose-rate (HDR) brachytherapy is an alternative strategy for those suitable for an interventional procedure. These approaches may result in high-precision targeted dose-escalated radiation treatment. We present two cases to illustrate these treatment strategies.

Methods

Study Design

Patients with localized prostate cancer and evidence of an intraprostatic lesion visible on mpMRI were enrolled onto a clinical trial (NCT01802242). Two treatment strategies, VMAT or HDR boost, were used and were chosen at the patient's and treating physician's discretion. MRI-guided biopsies and FM insertion were the same regardless of the treatment modality. This study was conducted under institutional research ethics approval for experimental studies on human participants and for clinical trial registration.

VMAT

EBRT consisted of image-guided VMAT to a total dose of 76 Gy in 38 fractions to the whole prostate (ie, clinical target volume [CTV76]), with an integrated boost to 95 Gy in the same number of fractions to the tumour (ie, CTV95).

HDR boost

Patients treated with HDR brachytherapy underwent a single implant to deliver 10 Gy in one fraction to the GTV, followed by VMAT within 1 week after the HDR boost, to a dose of 76 Gy in 38 fractions to the whole prostate (ie, CTV).

Study Procedures

This procedure was performed with the patients under anesthesia in a modified lithotomy position within a 3 T MR scanner (Verio; Siemens). An MRI-compatible

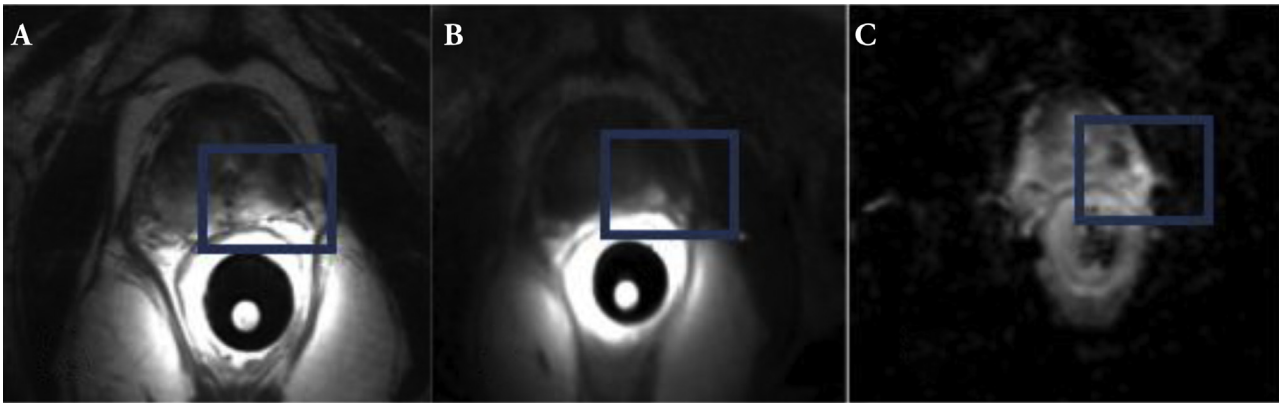

Figure 1. Multiparametric magnetic resonance imaging (mpMRI) sequences (from left to right). (A) T2-weighted (B) dynamic contrast-enhanced, and (C) apparent diffusion coefficient images taken during the interventional procedure depicting areas of high tumour density in the blue box. (Color version of figure is available online.)