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Adaptive Radiotherapy Enabled by MRI Guidance

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Abstract

Adaptive radiotherapy (ART) strategies systematically monitor variations in target and neighbouring structures to inform treatment-plan modification during radiotherapy. This is necessary because a single plan designed before treatment is insufficient to capture the actual dose delivered to the target and adjacent critical structures during the course of radiotherapy. Magnetic resonance imaging (MRI) provides superior soft-tissue image contrast over current standard X-ray-based technologies without additional radiation exposure. With integrated MRI and radiotherapy platforms permitting motion monitoring during treatment delivery, it is possible that adaption can be informed by real-time anatomical imaging. This allows greater treatment accuracy in terms of dose delivered to target with smaller, individualised treatment margins. The use of functional MRI sequences would permit ART to be informed by imaging biomarkers, so allowing both personalised geometric and biological adaption. In this review, we discuss ART solutions enabled by MRI guidance and its potential gains for our patients across tumour types.

Key words: Adaptive radiotherapy; gating; image guided; magnetic resonance imaging; radiotherapy planning; tracking

Search Strategy and Selection Criteria

An electronic literature search was carried out using PubMed and Web of Science databases. The final search was carried out in July 2018. Search terms included “radiotherapy”, “radiotherapy planning”, “adaptive radiotherapy”, “online adaptive radiotherapy”, “magnetic resonance”, “MR”, “MR-guided”, “radiotherapy tracking”, and “radiotherapy gating”. The search was restricted to those published in English with preference given to more recent studies. Selected studies were first screened by their title and/or abstract followed by full article review of relevant articles. A manual review of the reference list of relevant studies was also undertaken.

Introduction

The target for radiotherapy is dynamic. It varies in position, shape, size, and biology over a time frame that extends over seconds, days, and weeks (Figure 1). Reliance on a single pre-treatment planning computed tomography (CT) scan to capture this change over the treatment course is misplaced. Historically, to try and account for this geometric variation, large margins have been used to create the planning target volume (PTV) [1–3]. This, however, often limits dose escalation to tumoricidal levels because of concerns regarding collateral damage to adjacent normal structures [4,5].

Accepting that the PTV is a statistical construct to ensure that dose can be successfully delivered to the tumour, reliably decreasing PTV size is only possible when there is confidence in target positioning during treatment. Technologies that have enabled imaging in the treatment room have allowed gains to be made on this front, so overcoming, in part, the challenge of hitting an otherwise invisible target with an invisible beam. Image-guided radiotherapies (IGRTs), particularly those permitting soft-tissue visualisation, such as cone-beam CT (CBCT), prior to treatment delivery, have already demonstrated step-wise improvement in target coverage. This has been achieved using smaller margins and a subsequent reduction in integral

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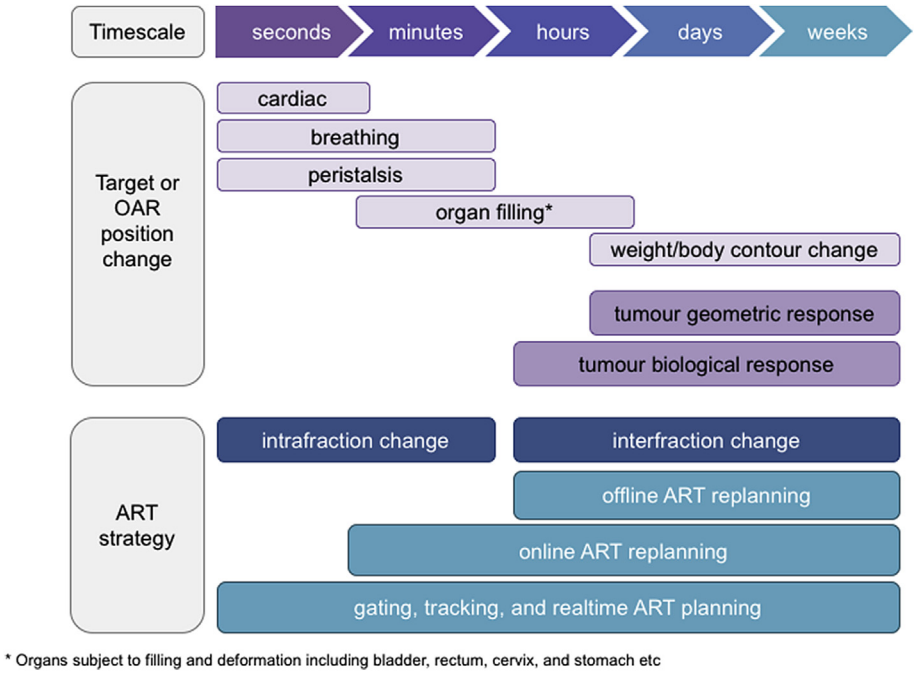

Fig 1. Timescales for adaptation and ART solutions implemented .

dose to surrounding tissues when compared to surrogates for target position such as skin tattoos or bony anatomy [6].

Adaptive radiotherapy (ART) is an umbrella term encompassing techniques that allow knowledge of patient-specific anatomical variations informed by IGRT to feedback into the plan and dose-delivery optimisation during the treatment course [7]. This ensures that the planned dose is delivered as accurately and precisely as possible according to the anatomy of the day. ART can be implemented broadly over three timescales (Figure 1): (1) offline between fractions, (2) online immediately prior to a fraction, and (3) in real-time during a fraction.

Offline ART monitors the position of the target during a limited number of fractions. It addresses systematic changes to some extent, but also allows opportunity for an individualised PTV margin to be applied based on acquired knowledge of the location of volumes of interest and patient set-up. Although adaptation is not informed by the exact position of the tumour at each fraction, the applied margins are often smaller than population derived margin recipes [8,9]. Online and real-time ART protocols modify the treatment plan while the patient remains on the couch. These strategies allow for a patient specific PTV to be created because they are informed by the actual change in anatomy seen for that fraction. As there is greater certainty to the true position of the tumour, an even smaller “safety” margin can be considered. The confidence in soft-tissue targeting at the time of radiotherapy delivery provides an opportunity to deliver higher radiation doses with tighter margins. In this review, we discuss ART solutions enabled by magnetic resonance imaging (MRI) guidance and it potential gains for our patients.

Will MRI-Guided Radiotherapy be the Ultimate Online IGRT Solution?

The persisting weakest link in the treatment chain for radiotherapy remains clinician-led target identification [10,11]. Repeated studies have demonstrated that gross tumour volume (GTV) and organ at risk (OARs) delineation variability between observers introduces systematic errors, which are larger than daily set-up uncertainties [12–14].

One of the most important factors responsible for the observed target variation is adequate imaging [12]. Compared to CT or CBCT, MRI offers superior soft-tissue definition with no associated radiation risk [15–17]. As a result, for many tumours diagnostic MRI improves inter- and intra-observer delineation consistency [12,18–20]. Observer variation also improves with the use of standardised guidelines, anatomy atlases, and auto-segmentation tools [21].

MRI delineated target volumes are often reported to be significantly different from those contoured on CT. Occasionally, MRI identifies targets larger than on CT because tumour that otherwise would have been missed is now seen [20]; however, most commonly, targets are reported to be smaller when delineated on MRI [18,19,22,23]. The resulting smaller MRI-derived target improves the therapeutic ratio so enabling dose escalation. For example, an MRI-delineated prostate, allows dose escalation of 2–7 Gy while maintaining the same rectal wall dose compared with a CT-delineated prostate [24]. Similarly, in cervical cancer, dose escalation is possible using an MRI-informed target with an associated 10–20% survival gain seen at 3 years with reduced gastrointestinal and urinary late morbidity [25].

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