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Overview

Motion Management for Radical Radiotherapy in Non-small Cell Lung Cancer

A.J. Cole *†, G.G. Hanna *†, S. Jain *†, J.M. O'Sullivan *†

* Northern Ireland Cancer Centre, Belfast, UK
† Centre for Cancer Research and Cell Biology, Queens University, Belfast, UK

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Abstract

Intrafraction tumour motion is an issue that is of increased interest in the era of image-guided radiotherapy. It is particularly relevant for non-small cell lung cancer, for which a number of recent developments are in use to aid with motion management in the delivery of radical radiotherapy. The ability to deliver hypofractionated ablative doses, such as in stereotactic radiotherapy, has been aided by improvements in the ability to analyse tumour motion and amend treatment delivery. In addition, accounting for tumour motion can enable dose escalation to occur by reducing the normal tissue being irradiated by virtue of a reduction in target volumes. Motion management for lung tumours incorporates five key components: imaging, breath-hold techniques, abdominal compression, respiratory tracking and respiratory gating. These will be described, together with the relevant benefits and associated complexities. Many studies have described improved dosimetric coverage and reduced normal tissue complication probability rates when using motion management techniques. Despite the widespread uptake of many of these techniques, there is a paucity of literature reporting improved outcome in overall survival and local control for patients whenever motion management techniques are used. This overview will review the extent of lung tumour motion, ways in which motion is detected and summarise the key methods used in motion management.

Key words: Four-dimensional computed tomography; gating; motion management; non-small cell lung cancer; radiotherapy; tracking

Statement of Search Strategies Used and Sources of Information

Articles were sourced through a structured literature search using the Medline/Pubmed database using the following search terms and their associated synonyms and Medical Subject Headings (MeSH): 4D-CT, radiotherapy, motion management, active breathing control, deep inspiration breath-hold, gating, tracking, image-guided radiotherapy, non-small cell lung cancer and respiratory motion. The search range was from 1946 to 2013 with priority given to publications within the last 15 years. Full articles were retrieved when the abstract was deemed relevant.

Introduction

The use of radiotherapy in lung cancer is increasing, with stereotactic ablative radiotherapy (SABR) now considered the preferential treatment for medically inoperable stage I non-small cell lung cancer (NSCLC) and a viable option for surgically operable patients requesting non-invasive treatment modalities [1]. Although SABR predates many recent technological advances, it has been assisted by newer techniques used to stage, plan and deliver treatment to patients. These advances include a variety of scanning and treatment modalities, including positron emission tomography (PET), four-dimensional computed tomography (4D-CT), intensity-modulated radiotherapy, volumetric modulated arc therapy and image-guided radiotherapy (IGRT). The underpinning dogma of delivering a high and preferentially tumouricidal dose to a target area coupled with a low dose to surrounding critical structures remains the goal in achieving the highest therapeutic ratio.

Author for correspondence: A.J. Cole, Clinical Oncology, Northern Ireland Cancer Centre, Belfast Health and Social Care Trust, 51 Lisburn Road, Belfast BT9 7AB, UK.
E-mail address: coleaidan@hotmail.com (A.J. Cole).

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An important restricting factor in modulating radiotherapy precisely to three-dimensional structures is the inherent presence of positional uncertainty; this can be affected by a number of factors, one of which is respiratory motion. Respiratory motion is a complex physiological mechanism that is affected by numerous patient-related issues, including co-existing pulmonary disease, tumour-related factors (atelectasis/effusion), concomitant infection, chemotherapeutic agents, cachexia and respiratory function modulators, e.g. dexamethasone, bronchodilators [2]. Failure to account for lung tumour motion secondary to respiration can lead to excessive dose to normal lung parenchyma, which is often the dose-limiting constraint for curative radiotherapy as well as tumour underdosage, which in turn can contribute to failure of local control [3].

Motion management techniques have been increasingly used in stereotactic radiotherapy to facilitate hypofractionated ablative doses leading to local control rates comparable with surgery [4]. The reduction in margins by strictly accounting for tumour motion can reduce toxicity to normal lung. In standard conformal radiotherapy, generic margins based on population statistics may lead to geometric miss and as such may contribute to suboptimal local control rates, as well as an increase in dose-limiting toxicities, such as pneumonitis [5,6]. Respiratory motion management can lead to a reduction in margins, but has many challenges in optimising the planning and delivery of radiation [7]. Although centres in the UK are embracing new technology to improve treatments, there is no standardised approach as to how best to immobilise patients, minimise motion and incorporate IGRT into these advanced radiotherapy techniques [8]. The need for prospective data is strengthened by practice in the USA, where these techniques are well established, but significant disparities exist in implementation and usage [9].

This overview will review the extent of lung tumour motion, ways in which motion is detected and summarise the key methods used in motion management for radical external beam radiotherapy for NSCLC.

Extent of Tumour Motion

To varying degrees, all organs within the thorax and abdomen are subject to changes in position due to respiratory motion. Of these, the lungs and, to a lesser extent, liver and breast are most affected [10]. Tumour motion can be measured in a number of ways, most commonly by use of fluoroscopy or 4D-CT [11], with or without radiographic fiducials or surrogates for tumour motion, such as the diaphragm [12,13]. A study by Seppenwoolde *et al.* [14] used gold fiducials inserted into or near tumours and tracked their motion using a real-time tracking system, imaging three-dimensional co-ordinates at 30 images per second. A summary of the motion pattern is shown in Figure 1. They concluded that tumour motion was greatest in the superior–inferior direction for unfixed tumours and for lesions close to the diaphragm. Other studies using a variety of imaging techniques verified these findings [14,15]. A number of other factors, including tumour size, fixity to underlying tissue and proximity to the heart, are also important [16,17].

Motion, although measurable, is not always predictable and hysteresis describes the phenomenon by which tumours can exhibit paradoxical motion on inspiration and expiration [18]. In addition, primary tumour motion does not have a direct relationship with involved or high-risk lymph nodes, which can influence subsequent motion management [19]. Pantarotto *et al.* [20] examined the motion of 100 lymph nodes in 41 patients, concluding that nodal motion >5 mm is common, as were offsets between primary tumour and mediastinal lymphadenopathy. Some nodal stations exhibited motion in excess of 1 cm, which would not be accounted for by standard isotropic margins [20]. It is important to note that cardiac motion can also have an influence on tumour motion, particularly for left lower lobe tumours [14].

Motion Management

Motion management can include a variety of techniques, such as respiratory control with breath-holding, abdominal compression plates and radiotherapy delivery techniques, such as gating and tracking [7]. The five most important components that overlap and interact to some degree are summarised in Figure 2. Both audio and audio-visual coaching to improve the reproducibility of the frequency and amplitude of breathing have shown high compliance and a significant reduction in the time to deliver treatments when combined with motion management [21–25]. A variety of immobilisation devices can be used to ensure the reproducibility of patient position, which is of particular importance in stereotactic radiotherapy. These include stereotactic frames, robotic-aided positioning devices and vacuum systems [26]. A summary of published studies using motion management strategies is shown in Table 1.

Imaging

Image acquisition without accounting for respiratory motion can lead to significant artefacts [36], which can influence target volume delineation, as well as positional and volumetric information [37,38]. Standard CT slices take less time to acquire than the average breathing cycle (4–6 sec) and can lead to step artefacts, partial projection and blurring of images [39]. This can lead to misrepresentation of the size, shape and position of the primary tumour [40]. Slow CT scans have been used to improve the imaging of the average organ position, but significant blurring of images can lead to difficulties in target delineation [41]. In an attempt to reduce artefacts associated with slow CT and more accurately define the trajectory of a tumour during respiratory motion, the development of respiratory correlated CT scanning was established [42].

4D-CT enables the correlation of CT scanning with the breathing cycle to allow analysis of an individual's