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Overview

Pitfalls and Challenges to Consider before Setting up a Lung Cancer Intensity-modulated Radiotherapy Service: A Review of the Reported Clinical Experience

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Abstract

Intensity-modulated radiotherapy (IMRT) is being increasingly used for the treatment of non-small cell lung cancer (NSCLC), despite the absence of published randomised controlled trials. Planning studies and retrospective series have shown a decrease in known predictors of lung toxicity (V20 and mean lung dose) and the maximum spinal cord dose. Potential dosimetric advantages, accessibility of technology, a desire to escalate dose or a need to meet normal organ dose constraints are some of the factors recognised as supporting the use of IMRT. However, IMRT may not be appropriate for all patients being treated with radical radiotherapy. Unique problems with using IMRT for NSCLC include organ and tumour motion because of breathing and the potential toxicity from low doses of radiotherapy to larger amounts of lung tissue. Caution should be exercised as there is a paucity of prospective data regarding the efficacy and safety of IMRT in lung cancer when compared with three-dimensional conformal radiotherapy and IMRT data from other cancer sites should not be extrapolated. This review looks at the use of IMRT in NSCLC, addresses the challenges and highlights the potential benefits of using this complex radiotherapy technique.

Key words: IMRT; intensity-modulated radiotherapy; lung cancer; non-small cell lung cancer; radiation pneumonitis; radiotherapy

Statement of Search Strategies Used and Sources of Information

The aim of this overview was to review the clinical experience of intensity-modulated radiotherapy (IMRT) for lung cancer after summarising the development of IMRT technique in this setting. In order to review the clinical experience of IMRT for lung cancer, a PUBMED search was carried out on 23 April 2014. The search was limited to articles in English print and used the following parameters: lung cancer AND clinical outcome AND IMRT (53 results); non-small cell lung cancer AND IMRT (148 results). This yielded 201 publications. Of the returned articles, we included studies reporting clinical outcome data after the use of IMRT in non-small cell lung cancer (NSCLC). References of the selected articles were also searched and further studies with relevant clinical data were identified and selected for this review. Relevant selected planning and dosimetric studies showing potential advantages of IMRT over three-dimensional conformal radiotherapy in lung cancer were examined and included. Case reports and hypofractionated stereotactic radiotherapy studies and studies on other tumour types were excluded. Where institutions have multiple publications, the previous publication was included only if it gave useful additional information. In total, five institutions have reported actual clinical outcome data on IMRT for NSCLC. Seven publications from five institutions were identified and included (Tables 3 and 4). Repeat analyses with a longer follow-up and more patients were available and were included from two institutions. Technical IMRT planning and delivery

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Table 1
Intensity-modulated radiotherapy (IMRT) for lung cancers: facts, problems and solutions

Fact	Practical problems	Answer/solution	Reference
High conformity of dose around target volume	Highly susceptible to systematic errors in delineation and geometric uncertainty	Adequate margins must be incorporated into the treatment plan	[35]
	Steep gradient with rapid fall-off at the edges of the target volumes	The quality assurance of immobilisation and treatment verification with appropriate image guided radiotherapy must be robust	[35]
Heterogeneous dose distribution	Single prescription points are unsatisfactory	A mean dose is prescribed to the target volume	[35,36]
Appropriate dose constraints may not be properly assigned to all the different tissues and organs in the path of the beams	Dose dumping (deposition of higher than usual dose of radiation at an unintended location) may be seen when critical structures are incompletely contoured	OAR contours must extend well beyond the cranial and caudal extent of the PTV	[35,39]
	Excess dose may be deposited in organs that are traditionally non-critical (such as heart) that do not require irradiation	Doses to the non-critical structures, such as skin or muscle tissue, should be monitored	[35]
		All relevant OARs should be contoured and dose constraints applied in the IMRT optimisation	
Critical structures (OARs) may be incompletely contoured	Non-coplanar fields may be assigned through critical structures and radiation passing through them will not be identified or represented in the DVHs	Coplanar beam arrangements are used by most planners for lung IMRT to minimise this problem	[35]
Unlike 3DCRT, with IMRT, the entire PTV is not always covered by the beam in all its segments IMRT may only irradiate a part of the target volume with any given segment of a field	Potential interplay between moving subfields (segments) and moving lung tumour is a matter of concern	The dosimetric effect of this interplay is probably less than 1% if the treatment is delivered over 30 fractions or more	[23–26]
		For similar fractionation, dose variation due to respiratory motion in IMRT is comparable to 3DCRT	[24]
		The effects of interplay are probably blurred or 'washed out' with multiple fields over a fractionated course of radiotherapy	[23–26]
		Various studies with fractionated IMRT schedules did not show unpredictable hot and cold spots within the target volumes because of interplay between tumour motion and MLC movement	[23–26]
Multiple beam angles from intensity modulation may increase the integral radiation dose delivered to the lungs	A higher mean lung dose and a larger volume of normal lung tissue receiving a greater low-dose radiation (low-dose bath) [21,41]	Clinically, this should not be of major concern in patients with locally advanced (stage III) non-small cell lung cancer; some of who would otherwise have received high dose palliative radiotherapy and would have a median survival of 9 months.	[11]
	The long-term clinical effects of this low-dose bath on breathing and gas exchange are not well understood		
Longer treatments using more monitor units may result in greater radiation leakage through the MLC leaves and other shielding, leading to a higher total body dose [35]	This could also lead to an increased incidence of secondary malignancies [42,43]		
Often large irregularly shaped target volumes	Off-axis delivery (using asymmetric jaws) of irregularly shaped fields is not routinely commissioned by physics departments for low density tissue and the delivery accuracy is therefore not known	Ongoing dosimetric audit is needed in individual departments to confirm that the dose distributions being delivered are accurate and reliable	[35,41,44]

OAR, organ at risk; 3DCRT, three-dimensional conformal radiotherapy; PTV, planning target volume; MLC, multileaf collimator; DVH, dose-volume histogram.

challenges and concerns in the setting of thoracic cancers were identified by studying the selected and relevant articles and published guidelines. Specific searches were carried out, pertaining to individual questions/problems about IMRT.

Introduction

Lung cancer is the leading cause of cancer-related death worldwide [1–3]. Non-small cell lung cancer (NSCLC) accounts for over three-quarters of all lung cancer cases.

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