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Original Article

Patterns of Failure after Intensity-modulated Radiotherapy in Head and Neck Squamous Cell Carcinoma using Compartmental Clinical Target Volume Delineation

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Abstract

Aims: To determine the pattern of disease recurrence in non-nasopharyngeal head and neck squamous cell carcinoma (HNSCC) patients treated with radical intensity-modulated radiotherapy (IMRT) with or without chemotherapy, and to correlate the sites of locoregional recurrence with radiotherapy target volumes.
Materials and methods: In total, 136 patients treated with radical IMRT with or without chemotherapy between 2008 and 2011 for non-nasopharyngeal HNSCC were retrospectively identified. A compartmental approach to clinical target volume (CTV) delineation was routinely utilised during this period and IMRT was delivered using a 5–7 angle step and shoot technique. Locoregional recurrences were reconstructed on the planning computed tomography scan by both deformable image coregistration and by visual assessment, and were analysed in relation to target volumes and dosimetry.
Results: The median follow-up was 31 (range 3–53) months. Two year local control, regional control, disease-free survival, distant metastasis-free survival and overall survival were 86, 93, 78, 89 and 79%, respectively. One hundred and twenty of 136 (88%) patients achieved a complete response to treatment and 7/120 (6%) have subsequently had a locoregional recurrence. Analysis of these recurrences revealed five to be infield; one to be marginal to the high-dose CTV; one to be out-of-field. Overall the marginal/out-of-field recurrence rate was 2/136 (1.5%).
Conclusions: IMRT utilising a compartmental approach to CTV delineation was associated with a low rate of marginal/out-of-field recurrence.

Key words: Chemotherapy; coregistration; head and neck cancer; intensity-modulated radiotherapy; recurrence pattern

Introduction

Intensity-modulated radiotherapy (IMRT) has been widely adopted for the treatment of head and neck squamous cell carcinoma (HNSCC) [1]. IMRT provides a highly conformal dose distribution with steep dose gradients. The rationale for the use of IMRT for HNSCC is that the dose distribution will improve the therapeutic ratio. This principle has been shown in studies using IMRT in the treatment of oropharyngeal cancer to spare the contralateral parotid gland with a consequent reduction in the severity of xerostomia [2,3]. IMRT may also improve tumour coverage in scenarios when conventional conformal radiotherapy techniques are limited by proximity of the tumour target to critical structures.

The inherent risk with the use of IMRT with steep dose gradients is the potential for geographical tumour miss, with subsequent locoregional recurrent disease. Target delineation has been described as the 'weakest link' in the radiotherapy process for HNSCC [4,5]. The high-dose clinical target volume (CTV) accounts for potential routes of microscopic spread of tumour. The use of IMRT techniques relies on accurate CTV delineation to avoid marginal tumour recurrences. Less conformal older non-IMRT techniques were more forgiving in cases of inaccurate target volume delineation. However, in the IMRT era there is no consensus on the optimal method of constructing a primary tumour CTV around the gross tumour volume (GTV) [6,7]. Within the UK, a recent survey of head and neck oncologists revealed wide variation in methods of primary tumour CTV

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delineation [7]. A volumetric method of geometric expansion with a margin from primary tumour GTV has been used most widely in many countries. Margins used for a volumetric expansion are very variable between institutions, for example varying from 0 to 20 mm [6]. By contrast, in line with the recent UK national clinical trials [2], we have used an anatomical/compartmental approach to the construction of the CTV around the primary tumour. This involves the construction of a CTV designed to encompass the relevant anatomical structure, for example the whole oropharynx. A compartmentally generated CTV is commonly larger than a CTV constructed by a volumetric expansion [8] and might be expected to minimise the risk of marginal recurrences.

Analysis of patterns of treatment failure is essential in the evaluation of the quality of target volume delineation. The location of the recurrence in relation to treatment volumes indicates the cause of treatment failure, i.e. an in-field recurrence suggests radioresistance, whereas a marginal or out-of-field failure indicates a geographical miss. We have previously reported patterns of failure in a cohort of 151 patients treated between 2004 and 2006 with three-dimensional conformal radiotherapy [9]. In our centre, IMRT was introduced for HNSCC in late 2008; in line with previous and ongoing UK trials we have adopted a compartmental approach to primary tumour delineation. The purpose of this study was to assess the pattern of failure after the introduction of IMRT with a compartmental approach to CTV delineation.

Materials and Methods

Study Design

A retrospective study was carried out using patient records, radiotherapy treatment plans and diagnostic imaging on patients who had been treated with IMRT with curative intent.

Study Population

IMRT was introduced for head and neck cancer patients at St. James's Institute of Oncology in December 2008. During this period, IMRT was used only for patients requiring bilateral neck irradiation. Records of consecutive patients treated with IMRT for head and neck cancer between December 2008 and December 2011 were reviewed. Inclusion criteria were: HNSCC, non-nasopharyngeal primary and treatment with curative intent. Patients treated with primary surgery were excluded, although patients who had neck dissections without treatment of the primary tumour were included.

Treatment Approach

Induction Chemotherapy

Induction chemotherapy (ICT) was used based on clinician preference, patient and tumour factors; in general, ICT was considered for patients with bulky disease. Standard ICT consisted of either TPF (docetaxel 75 mg/m^2 day 1, cisplatin 75 mg/m^2 day 1 and 5-fluorouracil 750 mg/m^2 days 2–5 three weekly) for selected fit patients [10] or PF (cisplatin 80 mg/m^2 day 1 and 5-fluorouracil 800 mg/m^2 days 2–5, three weekly) [11].

Concurrent Chemotherapy

Patients <70 years old were considered for concurrent chemotherapy. Standard concurrent chemotherapy was cisplatin 100 mg/m^2 days 1 and 29. Carboplatin AUC 4 was substituted for cisplatin if creatinine clearance was <55 ml/min.

Radiotherapy Treatment Planning

Patients were treated supine with a five-point thermoplastic mask. Planning computed tomography scans were acquired with intravenous contrast with 2 mm slices. The planning computed tomography dataset was transferred to the treatment planning system (Xio®, Electa and from 2010 Monaco®, Electa).

A compartmental approach to target volume delineation was adopted. The GTV was outlined as the primary tumour and clinically and/or radiologically involved lymph nodes. A primary tumour CTV was created to include at least GTV + 10 mm and the anatomical compartment, modified to anatomical boundaries to exclude air and/or bone without evidence of invasion. For example, for an oropharyngeal tumour, the whole oropharynx was included in the primary tumour CTV. The high-dose nodal CTV was constructed to include the whole involved nodal level. Nodal levels that did not include a radiologically abnormal lymph node were treated at an intermediate or a lower dose level according to clinician preference. The lymph node target routinely included levels 1b–V in the node-positive neck; nodal levels in a node-negative neck were selectively irradiated depending upon tumour site and disease extent according to published recommendations [12]. Retropharyngeal lymph nodes were routinely included in the target volume in cases with positive level II lymph nodes and involvement of the pharyngeal wall. The planning target volume (PTV) was created by auto-expansion of the CTV by 4 mm [9].

The standard radical dose was 70 Gy in 35 fractions to high-dose PTV, 63 Gy in 35 fractions to the intermediate risk PTV and 57 Gy in 35 fractions to the elective PTV. Organ at risk constraints were spinal canal maximum 48 Gy, brainstem maximum 54 Gy, larynx mean <45 Gy (excluding parts of the larynx within the PTV), contralateral parotid mean <26 Gy. Treatment was delivered with a 5–7 angle step and shoot IMRT technique.

Response Assessment and Follow-up

The tumour response was assessed 3–4 months after the completion of treatment. The response assessment routinely included clinical examination, panendoscopy and imaging. Biopsy was considered in the event of clinical or radiological suspicion. Patients were followed up with a physical examination every 6–8 weeks in the first year after treatment, every 3 months for an additional 2 years and every 6 months until discharge at 5 years.