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Original Article

Defining the Target in Cancer of the Oesophagus: Direct Radiotherapy Planning with Fluorodeoxyglucose Positron Emission Tomography-Computed Tomography

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Abstract

Aims: Target definition in radiotherapy treatment planning (RTP) of oesophageal cancer is challenging and guided by a combination of diagnostic modalities. This planning study aimed to evaluate the contribution of single positron emission tomography-computed tomography (PET-CT) in the treatment position to RTP.

Materials and methods: Nineteen patients referred for radiotherapy from April to December 2008 were retrospectively identified. Two sets of target volumes were delineated using the planning CT and the ^{18}F-fluoro-deoxy-D-glucose (^{18}F-FDG) PET-CT data sets, respectively. Target volumes were compared in length, volume and geographic conformality. Radiotherapy plans were generated and compared for both data sets.

Results: PET-CT planning target volume (PET-CT$_{PTV}$) was larger than the CT target (CT$_{PTV}$) in 12 cases and smaller in seven. The median PTV conformality index was 0.82 (range 0.44–0.98). Radiotherapy plans conforming to normal tissue dose constraints were achieved for both sets of PTV in 16 patients (three patients could not be treated to the prescription dose with either technique due to very large target volumes and significant risk of normal tissue toxicity). Previously undetected locoregional nodal involvement seen on PET-CT in three cases was localised and included in the PTV. In nine cases, the CT$_{PTV}$ plan delivered less than 95% dose to 95% of the PET-CT$_{PTV}$, raising concern about potential for geographical miss.

Conclusion: A single scan with diagnostic PET-CT in the treatment position for RTP allows greater confidence in anatomical localisation and interpretation of biological information. The use of PET-CT may result in larger PTV volumes in selected cases, but did not exclude patients from radical treatment within accepted normal tissue tolerance.

Key words: Oesophageal cancer; PET-CT; radiotherapy planning

Introduction

The incidence of oesophageal cancer in the UK is increasing, with 14.1 and 5.2 cases per 100 000 population in men and women, respectively, in England in 2011 compared with 8.8 and 4.8 before 1977 [1,2]. Chemoradiotherapy is standard care for patients who are not candidates for curative surgery, and may be given with curative intent or for palliation of locally advanced disease [3,4]. About 60–70% of patients with oesophageal cancer in the UK receive radiotherapy as part of their management (data provided by The National Cancer Services Analysis Team in March 2011).

Defining the primary target in the oesophagus has historically been difficult. Two-dimensional radiotherapy treatment planning (RTP) used oral radio-opaque contrast to visualise the stricture, but identifying the clinical and subclinical tumour extent was challenging. Planning target volume (PTV) margins of up to 5 cm were applied superior and inferior of the gross tumour volume (GTV), resulting in long treatment fields and limiting the dose that could safely be delivered [5]. Current practice has evolved to include diagnostic modalities, such as endoscopy, endoscopic

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ultrasound (EUS) and computed tomography (CT) to stage and localise the disease more confidently [6]. A pathological analysis of surgical specimens showed that the superior–inferior extent of microscopic spread within the oesophagus was less than 30 mm in 94% of cases [7]. GTV to PTV margins of 3 cm superior–inferiorly and 1.5 cm circumferentially were adequate in one study where CT and EUS were used to define the GTV, with 96% of local recurrences occurring in the treatment field [8]. The UK national SCOPE 1 trial, a randomised phase II/III trial of chemoradiation with or without cituximab, had an important impact to standardise radiotherapy planning for oesophageal cancer, mandating the use of intravenous contrast and EUS for target definition [9]. These developments are encouraging, but poor soft tissue discrimination of the oesophagus and adjacent lymph nodes on CT, and difficulty relating endoscopic findings to CT images, remain limiting factors.

^{18}F-fluoro-deoxy-D-glucose (^{18}F-FDG) positron emission tomography (PET) is an established imaging modality in the diagnosis and staging of many cancer sites and an emerging modality in RTP. PET adds data on the biological activity of tumours and has the potential to increase the accuracy of GTV delineation in many tumour types [10–16]. FDG-PET has 95% sensitivity in detecting the primary oesophageal carcinoma and provides a close estimation of tumour length when compared with oesophageal resection specimens [17–19]. Combination PET-CT is superior in detecting distant metastases compared with CT alone [19,20] and more accurate than CT and EUS in evaluating regional lymphadenopathy [15,19,21,22].

Data on the use of PET-CT for oesophageal cancer RTP are emerging. There are a few published studies, comprising small series, and two recent systematic reviews, both concluding that this technique needs further validation [23,24]. Published series consistently show that PET-CT significantly affects the size and anatomical localisation of the GTV, as well as the detection of unsuspected nodal involvement [25–32]. It is not yet clear whether the use of PET-CT in this setting will translate into therapeutic gain. In view of the increasing demand for oesophageal radiotherapy in the UK and the current resource restrictions in PET-CT availability, the use of PET-CT in this patient group needs to be justified, prioritised and integrated into the therapeutic pathway to allow optimal use of the biological data.

In 2005, the radiotherapy department at University College London Hospital secured access to a PET-CT scanner through charitable funding. Following a feasibility study, the patient pathway was simplified and from April 2008 all oesophageal staging PET-CT scans were acquired in the radiotherapy treatment position, facilitating direct PET-CT RTP. The aim of this retrospective planning study was to qualify and quantify the contribution of PET-CT to oesophageal RTP in terms of target volume delineation and plan dosimetry. We hope to contribute to the growing evidence base in this area. In recognition of a limited PET-CT provision for RTP in the UK, a secondary objective was to investigate whether a subset of oesophageal cancer patients could be identified as more likely to benefit from this technique.

Materials and Methods

Cases

Patients referred for radical or high-dose palliative chemoradiotherapy for thoracic oesophageal carcinoma and who had a planning PET-CT scan carried out between April and December 2008, were retrospectively identified. There were no exclusion criteria. Radiotherapy planning data were anonymised. Information on age, gender, histological subtype, cancer stage, the site of the primary tumour and treatment intent at referral was recorded for each patient.

Immobilisation and Positron Emission Tomography-Computed Tomography Scanning

Before FDG injection, an individualised patient immobilisation device was made, taking the PET-CT bore size restrictions into account. Patients fasted for 6 h before a standard adult dose injection of 400 MBq FDG. Uptake time was 60 min. A whole body staging FDG-PET-CT scan was acquired in the planned radiotherapy treatment position (supine with arms raised above the head) with radiotherapy immobilisation *in situ* (Medtech extended wing board and Q-Fix vacuum bag) and reference tattoos applied (one anterior and two lateral thorax tattoos). A GE Discovery DST scanner, with an external LAP laser system, was used. The non-contrast helical CT scan range was from orbits to groin, with the reference tattoo position marked. The PET data were subsequently acquired with the patient position and table vertical unchanged, in 4 min/13 cm cranio-caudal sections using the same scan range and typically six to seven table positions. The automatically co-registered PET-CT data were sent by DICOM (Digital Imaging and Communications in Medicine) as a single data set to a GE Advantage Windows (ADW) radiotherapy workstation, where the functional PET-CT data could be viewed, manipulated and delineated.

Target Volumes

The target volume contouring was carried out by one clinical oncologist.

Biological Target Volume (BTV)

The PET data were interpreted by an experienced consultant nuclear medicine physician who delineated the area of suspicious biological activity (the BTV) as a structure on the ADW workstation using visual thresholding. This method was selected as there is no validated evidence to indicate that automated contouring is reliable in this setting [33]. The same nuclear medicine physician delineated the BTV for the whole cohort to ensure consistency between cases.