



## Original Article

# Combination External Beam Radiotherapy and Intraluminal Brachytherapy for Non-radical Treatment of Oesophageal Carcinoma in Patients not Suitable for Surgery or Chemoradiation



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## Abstract

**Aims:** This single-centre retrospective study evaluated combination external beam radiotherapy and high dose rate brachytherapy for patients in whom radical treatment was appropriate but comorbidity or frailty excluded this as an option.

**Materials and methods:** In total, 59 patients were selected for a combined approach and treated between October 2000 and October 2011; 68% were male. The median age was 77 years (range 53–88 years); 66% had adenocarcinoma, 31% squamous cell carcinoma. Tumour stage: I: 20%, II: 43%, III: 32% and IV: 3%. External beam radiotherapy doses of either 27 Gy/six fractions or 30 Gy/10 fractions were delivered, followed by high dose rate brachytherapy at doses of either 10 or 15 Gy utilising an iridium 192 source at 1 cm.

**Results:** The median overall survival of all treated patients was 12.3 months; 1, 2 and 3 year survival rates were 51, 19 and 7%, respectively. Patients with stage I disease had a median survival of 16 months compared with 10 months for patients with stage III disease ( $P = 0.036$ ). The pretreatment dysphagia score was associated with survival ( $P = 0.021$ ).

**Conclusions:** This study shows the value of a purely radiation-based approach in a selected population. Treatment is deliverable with excellent compliance and the median survival compares favourably with unselected patients treated palliatively in our institution.

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**Key words:** HDR brachytherapy; hypofractionated radiotherapy; oesophagus; survival

## Introduction

The prognosis of oesophageal carcinoma remains poor, with 5 year survival rates in the region of 10% [1]. It is therefore important that the morbidity associated with a particular treatment modality is balanced against the probable benefits to the patient in terms of both survival and relief from dysphagia.

Current guidelines recommend a multimodality treatment approach depending on the patient's fitness, tumour histology and stage, with surgical resection the mainstay of curative therapy [2]. However, even in localised disease, 5 year overall survival rates are 20–25% [3].

Fewer than 20% of patients are amenable to radical surgery due to advanced stage of disease and significant comorbidity at presentation [4]. A surgical approach in patients over the age of 70 years risks potentially higher complications [5], with operative morbidity in the region of 40% [4] and mortality ranging from 4.7 to 7.2% [6].

Chemoradiation (CRT) can be used as an alternative definitive therapy in patients with localised or locally advanced oesophageal carcinoma. Trials have shown 5 year overall survival rates in the region of 25–30% [7,8], which are comparable with surgical series [9]. Median survival ranges from 14 to 18 months, with 2 year overall survival rates of 35–40% [10]. The recent results from the SCOPE 1 study showed a median overall survival in the chemoradiation arm of 25.4 months after the initial administration of two cycles of neoadjuvant chemotherapy [11].

However, CRT causes significant acute toxicity [12]. In the Radiation Therapy Oncology Group (RTOG) 85-01 study

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[8,13], the incidence of grade 3 and grade 4 toxicity was 44 and 20%, respectively. In a further retrospective analysis [14], 29% of patients required non-elective hospital admission, with 20% requiring feeding assistance.

There is therefore currently no standard treatment option that achieves effective palliation of symptoms with significant prolongation of survival in those for whom radical treatment options are not deemed appropriate.

The results of radical radiotherapy alone as a curative option in early stage disease have been disappointing, with 5 year survival rates not exceeding 10% and median survival of about 9 months [13,15]. One study utilising radical radiotherapy alone in a highly selected population showed a median overall survival of 15 months [16].

An influential study suggested that dose escalation with high dose rate brachytherapy (HDRBT) resulted in significant toxicity (oesophagitis, ulceration and stricture formation) with no survival benefit in advanced disease [17]. About 30% of patients do not complete therapy due to treatment morbidity [18].

Current palliative treatment options include hypofractionated external beam radiotherapy (EBRT) regimens, single fraction or fractionated HDRBT and/or stent insertion. These have poor survival outcomes (4–7 months) with the focus on achieving local symptom control [19–22]. However, it has been shown that both EBRT and HDRBT as sole or combined modality treatment offer superior palliation compared with stent insertion alone [21,23].

Recent findings from The National Oesophago-gastric Audit, which aims to assess the care pathway and the outcomes for individual patients with oesophago-gastric cancer in England and Wales, has shown significant variation and possible under-use of HDRBT, with only 54% of cancer networks reporting access to this modality [24].

This present single-centre retrospective study evaluated a combination of EBRT and HDRBT for patients in whom standard radical treatment options (with surgery or chemoradiation) were potentially appropriate, but comorbidity and frailty excluded this as an option. The aim was to deliver a high radiation dose to the primary tumour, which is well tolerated and could potentially achieve improved survival outcomes.

## Materials and Methods

### *Patient Population*

The study population comprised 59 patients with histologically confirmed oesophageal cancer treated with EBRT and HDRBT at Mount Vernon Cancer Centre between October 2000 and November 2011. A retrospective analysis used information from patient medical records, pathology databases and the electronic imaging system.

All patients had been discussed in a multidisciplinary setting in which standard radical therapies had been discounted. Most (66%) were deemed medically unfit due to frailty and/or significant comorbidity; 15% had extensive disease that was considered unresectable; 8% declined

surgery; 6% had severe toxicity to initial neoadjuvant chemotherapy; 3% has more than one active primary malignancy at the time of diagnosis.

A decision was made to treat with hypofractionated EBRT initially. Patients were subsequently selected for an HDRBT boost if they had localised/locally advanced disease, tolerated EBRT and achieved good symptomatic benefit with no significant clinical deterioration. In total, 59 patients were selected for the combined radiation approach from 1005 patients treated initially with EBRT.

### *Subgroups of Patients, Definitions and Description of Treatment*

All patients were staged according to the 7th TNM classification of malignant tumours by the American Joint Committee on Cancer [25]. Classification was based on the results of a physical examination, oesophageal endoscopy with biopsies and computerised tomography of the thorax, abdomen and pelvis, which was carried out in all patients. Endoscopic ultrasound was carried out in seven patients (12%). Positron emission tomography was carried out in 34 patients (58%). Six patients (10%) had laparoscopic staging and one patient underwent mediastinoscopy before treatment.

Performance status was graded 0–3 according to the Eastern Cooperative Oncology Group (ECOG) scoring system [26]. Medical comorbidities were graded according to the Adult Comorbidity Evaluation – 27 (ACE-27) index [27].

The presenting symptoms were recorded and dysphagia scored 0–4 according to the degree of severity [28], before and after treatment (6 weeks after completion). Two patients required oesophageal stent insertion before embarking on radiotherapy and another patient required endoscopic dilatation.

Tumour length was only recorded in a small proportion of patients' records. Brachytherapy volume length was used as a surrogate for tumour length as patients were treated universally with a 2 cm margin both cranially and caudally beyond the macroscopic borders of the tumour. Patients were stratified according to treatment length (<10 cm or ≥10 cm).

### *Radiation Treatment*

Ninety-four per cent of patients received EBRT followed by a HDRBT boost. The remainder received HDRBT either as a single treatment or fractionated. Until 2008, patients receiving EBRT underwent two-dimensional radiation treatment planning. A barium swallow was used during simulation to aid tumour localisation, specifically to assess the craniocaudal and axial extent of the oesophageal lesion. Since 2008, computed tomography scans were carried out routinely using 3 mm slices to allow for 'virtual simulation'. Margins of 2–3 cm laterally and 3–5 cm craniocaudally were applied to create the treatment field. EBRT was delivered using a high energy linear accelerator using 6 or 10 MV photon beams using anteroposterior parallel opposed fields prescribed to the mid-plane dose.

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