REPORTS OF PRACTICAL ONCOLOGY AND RADIOTHERAPY 20 (2015) 135–140

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.elsevier.com/locate/rpor

Original research article

Is dose escalation achievable for esophageal carcinoma?

*Laure Vieillevigne**, *Marie Vidal*, *Françoise Izar*, *Michel Rives*

Institut Claudius Regaud, Institut Universitaire du Cancer de Toulouse Oncopole, Radiotherapy Department, France

ARTICLE INFO

Article history:
Received 24 July 2014
Received in revised form
14 November 2014
Accepted 11 December 2014

Keywords:
Rapid arc
Tomotherapy
Dose escalation
Esophageal cancer

ABSTRACT

Aim: To investigate the feasibility of dose escalation using rapid arc (RA) and Helical Tomotherapy (HT) for patients with upper, middle and distal esophageal carcinomas, even for large tumor volumes.

Background: In esophageal cancer, for patients with exclusive radio-chemotherapy, local disease control remains poor. Planning study with dose escalation was done for two sophisticated modulated radiotherapy techniques: Rapid arc against Tomotherapy.

Materials and methods: Six patients treated with a RA simultaneous integrated boost (SIB) of 60 Gy were re-planned for RA and HT techniques with a SIB dose escalated to 70 Gy. Dose volume histogram statistics, conformity indices and homogeneity indices were analyzed. For a given set of normal tissue constraints, the capability of each treatment modality to increase the GTV dose to 70 Gy was investigated.

Results: Either HT or VMAT may be used to escalate the dose delivered in esophageal tumors while maintaining the spinal cord, lung and heart doses within tolerance. Adequate target coverage was achieved by both techniques. Typically, HT achieved better lung sparing and PTV coverage than did RA.

Conclusions: Dose escalation for esophageal cancer becomes clinically feasible with the use of RA and HT. This promising result could be explored in a carefully controlled clinical study which considered normal tissue complications and tumor control as endpoints.

1. Background

In Europe, the incidence of esophageal cancer is rising, especially the number of adenocarcinoma cases, located principally in the mid- or distal esophagus. Multimodality treatment strategies, such as chemo-radiotherapy[1] that can be associated with surgery or radiotherapy (pre or post-operatively), are generally the standard treatment. In locally advanced tumor, long term survival remains poor. For the cohort of patients with unresectable esophageal cancer studied by Settle,[2] 75% of radiation therapy failures occurred within the gross tumor volume (GTV). Despite recent advances in radiation planning, tumor imaging, and radiation delivery the radiotherapy techniques and doses used for treating esophageal cancer have remained relatively

* *Correspondence to*: 1, avenue Irène Joliot Curie, 31059 Toulouse, France. Tel.: +33 5 31 15 54 78.
E-mail address: vieillevigne.laure@iuct-oncopole.fr (L. Vieillevigne).

http://dx.doi.org/10.1016/j.rpor.2014.12.006

Table 1 – Summary of patient characteristics.

Patient	CT extent	Staging	PTV_2 (cm^3)	PTV_1 (cm^3)
1	Mid-esophagus	T3N1	119.0	651.7
2	Upper-esophagus	T3N1	147.4	821.5
3	Mid-esophagus	T3N1	145.5	548.7
4[a]	Mid-esophagus	T1N0	117.4	386.3
5	Distal-esophagus	T3N1	286.6	957.9
6	Mid-esophagus	T2N0	132.6	434.6

[a] Against medical indication to surgery.

unchanged. In esophageal cancer, for patients with exclusive radio-chemotherapy, local disease control, especially within the GTV, remains poor and problematic.

Radiotherapy of the esophagus is challenging because the tumor is surrounded by a host of organs at risk (OAR) including the lungs, heart and spinal cord. However, sophisticated modulated radiotherapy techniques allow improved dose-sparing of these structures.

Several dosimetric studies[3–6] have shown that, compared with standard three-dimensional conformal radiotherapy (3D CRT), intensity modulated radiotherapy (IMRT) can lower the dose to organs at risk (OARs) in the esophageal region without compromising target coverage.

Volumetric modulated arc therapy (VMAT) is an innovative technology which has recently been introduced. RapidArc (RA) is a method of VMAT based on the work of Otto.[7] In RapidArc, the dose rate, MLC positions and gantry rotation speed are simultaneously optimized by an iterative inverse process. VMAT can provide similar or even better OAR sparing and PTV coverage than IMRT with a shorter delivery time.[8–12] Helical Tomotherapy (HT) (TomoTherapy Inc., Madison, WI) is a modality for delivering IMRT treatments using a rotating linear accelerator.

This study investigates whether it is possible to deliver curative esophageal doses using HT and RA. In head and neck cancer, 70 Gy delivered in 35 fractions to the PTV is considered to be a curative dose.

Most published dosimetric studies of esophageal cancer consider lower prescribed doses,[13,14] for example Martin et al.[5] published a comparison of helical tomotherapy, RapidArc with prescriptions ranging from 45 to 60 Gy. Logically, the demonstrated benefits of radiation dose escalation for tumors at other anatomic sites in terms of improved local control and survival could be expected to apply to esophageal cancer as well. The standard esophageal prescribed dose of 50.4 Gy, published by RTOG[15] has been accepted for many years. Nevertheless, Zhang et al.[16] reported that higher doses of radiation were associated with decreased locoregional recurrence and increased survival. Hurmuzlu et al.[17] reported a positive correlation between local tumor control and high dose RT.

2. Aim

The aim of this study was to evaluate the possibility of escalating the dose to the PTV while respecting the dose constraints to organs at risk, using RA or HT. In our department, the standard prescription is based on a RA Simultaneaous Integrated Boost (SIB) delivering 60 Gy.

We compared dosimetric data between three Simultaneous Integrated Boot (SIB) modulated plans for medium and large targets in esophageal cancer:

1. The RA plan used for patient treatment, with our standard prescription dose of 60 Gy.
2. A second RA plan, dose-escalated to 70 Gy.
3. A HT plan, dose-escalated to 70 Gy.

3. Materials and methods

3.1. *Patient selection – contouring*

This study considered six patients with locally upper, middle or distal esophageal carcinomas. Table 1 summarizes the characteristics of the patients. All patients had large and long targets, with PTV volumes ranging from 386 cc to 957 cc. Each patient underwent a computed tomography scan with a slice thickness of 2.5 mm. The gross tumor volume (GTV) and involved lymph nodes were outlined by the radiation oncologist using information from fused PET/CT data, endoscopic reports and CT diagnosis images. The clinical target volume (CTV) was derived from the GTV by adding a 3D margin of 1 cm except in inferior and superior where 3 cm was applied. For each patient, two planning target volumes, PTV1 and PTV2, were generated. PTV1 consisted of the CTV plus a 1 cm margin. PTV2 consisted of the GTV plus a 1 cm margin. These two PTVs were used in the dose prescription as outlined in the subsection below. The relevant OARs were: the right and left lung, the whole lungs, the heart, the liver and the spinal canal. All of these OARs were outlined by the oncologist.

As outlined in the introduction, for each patient, three treatment plans were optimized:

1. A RA (RA SIB 48/60) plan with our standard dose of 60 Gy, delivering 60 Gy to PTV2 and 48 Gy to PTV1 in 30 fractions. This plan was delivered clinically.
2. A further RA plan (RA SIB 56/70) delivering 70 Gy to PTV2 and 56 Gy to PTV1 in 35 fractions.
3. A HT plan (HT SIB 56/70) delivering 70 Gy to PTV2 and 56 Gy to PTV1 in 35 fractions.

For all the plans, normalization was set to the median dose to the PTV volume receiving the highest dose prescription (PTV2) for compliance with the International Commission on Radiation Units and Measurements (ICRU) report 83 recommendations.[18]