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Oesophagus IMRT

Feasibility of using intensity-modulated radiotherapy to improve lung sparing in treatment planning for distal esophageal cancer

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Abstract

***Background and purpose*: To evaluate the feasibility whether intensity-modulated radiotherapy (IMRT) can be used to reduce doses to normal lung than three-dimensional conformal radiotherapy (3DCRT) in treating distal esophageal malignancies.**

***Patients and methods*: Ten patient cases with cancer of the distal esophagus were selected for a retrospective treatment-planning study. IMRT plans using four, seven, and nine beams (4B, 7B, and 9B) were developed for each patient and compared with the 3DCRT plan used clinically. IMRT and 3DCRT plans were evaluated with respect to PTV coverage and dose-volumes to irradiated normal structures, with statistical comparison made between the two types of plans using the Wilcoxon matched-pair signed-rank test.**

***Results*: IMRT plans (4B, 7B, 9B) reduced total lung volume treated above 10 Gy (V_{10}), 20 Gy (V_{20}), mean lung dose (MLD), biological effective volume (V_{eff}), and lung integral dose ($P<0.05$). The median absolute improvement with IMRT over 3DCRT was approximately 10% for V_{10}, 5% for V_{20}, and 2.5 Gy for MLD. IMRT improved the PTV heterogeneity ($P<0.05$), yet conformity was better with 7B–9B IMRT plans. No clinically meaningful differences were observed with respect to the irradiated volumes of spinal cord, heart, liver, or total body integral doses.**

***Conclusions*: Dose-volume of exposed normal lung can be reduced with IMRT, though clinical investigations are warranted to assess IMRT treatment outcome of esophagus cancers.**

Keywords: Esophageal cancer; Intensity-modulated radiotherapy; Three-dimensional conformal radiotherapy; Treatment planning

Treatment of esophageal cancer, which has a 5-year overall survival rate of 20–25% [1–3], traditionally involves chemoradiation for inoperable or unresectable disease or preoperative chemoradiation for operable disease [1–3]. Because the locoregional persistence or failure rate after chemoradiation is approximately 50% [1,3], better local treatment through radiotherapy may be needed to improve the overall treatment outcome. The goal of radiotherapy for esophageal cancer is to ensure appropriate coverage of the targeted structures while minimizing irradiation of normal tissues. One study found higher rates of postoperative pulmonary complications, such as pneumonia and acute respiratory distress syndrome, when higher lung volumes received low doses of lung radiation preoperatively: the pulmonary complication rate was 35% when the volume of lung receiving $\geq$10 Gy (V_{10}) was $\geq$40 and 8% when V_{10} was $<$ 40% ($P=0.014$) [4]. In that study, the treatment plan used conventional radiotherapy techniques, usually two-dimensional techniques using simulation films. Three-dimensional conformal radiotherapy (3DCRT) techniques have been shown to improve tumor targeting and to reduce irradiation of surrounding normal tissues, especially the lung [5].

Further improvement on dose conformity and normal tissue sparing can be accomplished by using intensity-modulated radiotherapy (IMRT) [6]. With IMRT, the possible gains over 3DCRT could come from reduced toxicity and delivery of a higher dose to target volumes. Use of IMRT for specific disease sites, including the prostate and the head and neck, has been investigated extensively and has become part of standard practice at many institutions [6]. However, very few studies have assessed whether IMRT is suitable or effective for treating esophageal cancer, partly because of

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the concern that IMRT may spread radiation at low doses to large volumes of normal lung tissue, which could be detrimental to radiosensitive structures. Only three reports have been published so far on the use of IMRT for esophageal cancer [7–9]. In two earlier studies [7,8], Nutting et al. showed 9B-IMRT plans were equivalent compared with 3DCRT plans regarding planning target volume (PTV), dose homogeneity and mean lung dose (MLD). However, 4B-IMRT plans with the same beam orientation as the 3DCRT plans increased PTV dose homogeneity and reduced the mean lung dose. A more recent report from Wu et al. [9] found that IMRT could be an effective tool to reduce volume of lung irradiated above 25 Gy for mid-thoracic esophageal cancers. Apparently, more extensive studies are needed to explore the potential gains of IMRT with respect to dosimetric improvements, before embarking on a clinical trial.

In this work, we completed a pilot study investigating the feasibility of using IMRT for cases of distal esophageal cancers, which typically involves higher lung volume being irradiated than cervical esophageal cancers. We determined whether IMRT could reduce dose delivered to normal lung than 3DCRT. Three types of IMRT beam arrangements were also made to assess optimal beam angles. Through this study, we intended to establish IMRT treatment strategies for esophagus cancers, and obtain preliminary results for designing future clinical trials.

Patients and methods

Ten patients who underwent treatment for esophageal cancer were selected from our existing patient population. Because the anatomy of distal esophageal cancers only varies slightly from patient to patient, these 10 cases were sufficient to represent typical anatomies for this group of patients. The patient identifiers were removed in accordance with an Institutional Review Board-approved retrospective study protocol. All of the patients had tumors involving the distal esophagus and gastroesophageal junction. Eight patients had stage III disease, one had stage IIB disease, and one had stage IVA disease. Through treatment simulation session, CT images of the entire thorax and upper abdomen were obtained using 3-mm slice spacing, including the entire liver and both kidneys. Images were obtained with the patient in the supine position. Gross tumor volume (GTV) was determined and reviewed by the attending radiation oncologist. Clinical target volume (CTV) was expanded with a 2-cm radial expansion and a 5-cm superior–inferior expansion, which followed our clinical guideline. PTV was defined as an additional 0.5-cm expansion beyond CTV. The median PTV was 899 cc (range, 585–1264 cc). Pinnacle treatment-planning system (version 6.0i; Philips Medical Systems North America, Andover, MA, USA) with collapsed cone convolution algorithm and heterogeneity correction was used for dose calculations.

Four types of treatment plans were generated for each patient case: 3DCRT, 4B-IMRT, 7B-IMRT, and 9B-IMRT. Most of the 3DCRT plans had the traditional four- beam arrangement with anteroposterior (AP), posteroanterior (PA), and two posterior oblique fields, but some used two parallel opposed oblique fields or an anterior and posterior oblique field to avoid the spinal cord. Typical oblique angles were 150 or 210° from the posterior side. The 3DCRT plans used clinically to treat the patients served as the comparison group; these plans were further renormalized to have the same PTV prescription as that of the IMRT plan and were approved to be clinically acceptable by the attending physician. The target dose was 50.4 Gy delivered in 28 fractions prescribed to 95% coverage of the PTV with concurrent chemotherapy. Mean PTV dose was 51.8 Gy in average for the 10 cases.

The 4B-IMRT plan used the same beam orientations as the four-beam 3DCRT plan. The intention of using the identical beam angles as the 3DCRT plans was to assess the effect of intensity modulation alone for the treatment. The 9B-IMRT plan was generated using equispaced (every 40°) beams, whereas the 7B-IMRT plan was generated using an equispaced nine-beam arrangement but without the two lateral beams (80 and 280°). These two laterally oriented beam angles may cause more lung exposure along the beam paths and thus may not be ideal for treatment of esophageal cancer. All IMRT plans were generated with 6MV photon beams with the above beam-angle template to minimize confounding factors such as manipulation of the beam orientation or beam energy. Because traditional issues of target localization, such as setup error and motion, are of concern in treatment planning, the *same PTV* that was considered adequate to address these issues in 3DCRT was used in IMRT. Using the same PTV allowed direct comparison of results from 3DCRT and IMRT plans without bias due to differences in planning margins.

The goals for inverse planning with IMRT were to ensure 95% coverage of the PTV to the prescribed dose (50.4 Gy at 1.8 Gy per fraction) while keeping the dose delivered to other normal structures, such as the lung, spinal cord, heart, and liver, within normally accepted tolerances. The treatment-planning parameters used to ensure coverage of the PTV were as follows: minimum dose of 48 Gy to 100% volume; maximum dose of 65 Gy to 5% of volume. Occasionally, a fictitious structure called 'expanded PTV' (i.e. PTV uniformly expanded by 1 cm) was created and prescribed $\geq$45 Gy to ensure adequate coverage of the PTV if necessary.

For the total lung, the planning objectives of V_{10} and V_{20} were generally assigned a level 10–20% lower than the median value of the 3DCRT plans (in absolute percentage of the lung volume at 10 and 20 Gy). More explicitly, with the 3DCRT plans, the DVHs for total lung were computed from which, V_{10} and V_{20} were deducted by 10–20% and were used as the planning goal for the corresponding IMRT plans. The maximum spinal cord dose used in the inverse planning was 45 Gy. Another fictitious structure named 'expanded spinal cord' (i.e. uniform expansion of the spinal cord by 1 cm) was created and prescribed a maximum of 40 Gy to ensure acceptable spinal cord doses and an additional geometric margin for the cord. For the heart, the planning goals were set to reduce V_{40} and V_{50} by 10–20% (in absolute percentage of the heart volume) than the median values of the 3DCRT plans. In general, V_{40} and V_{50} were kept to $<$50 and 30%, respectively, for the heart. For the liver, V_{30} was kept to $<$30% and no more than absolute 10% greater than the median value of the 3DCRT plans. To minimize hot spots