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Comparison of Toxicity between Intensity-Modulated Radiation Therapy and 3-Dimensional Conformal Radiotherapy for Locally Advanced Non-Small Cell Lung Cancer

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Abstract

Background—The role of intensity-modulated radiation therapy (IMRT) in reducing treatment-related toxicity for locally advanced non-small cell lung cancer (NSCLC) remains incompletely defined. We compared acute toxicity and oncologic outcomes in a large cohort of patients treated with IMRT or 3D conformal radiation therapy (3DCRT), with or without elective nodal irradiation (ENI).

Methods—A single-institution retrospective review was performed evaluating 145 consecutive patients with histologically-confirmed stage III NSCLC treated with definitive chemoradiation. Sixty-five (44.8%) were treated with 3DCRT using ENI, 43 (30.0%) with 3DCRT using involved-field radiotherapy (IFRT), and 37 (25.5%) with IMRT using IFRT. All patients received concurrent chemotherapy. Comparison of acute toxicities by treatment technique (IMRT vs. 3DCRT) and extent of nodal irradiation (3DCRT-IFRT vs. 3DCRT-ENI) was performed for grade ≥2 esophagitis or pneumonitis, number of acute hospitalizations, incidence of opioid requirement, PEG utilization, and percent weight loss during treatment. Local control and overall survival were analyzed with the Kaplan-Meier method.

Results—We identified no significant differences in any measures of acute toxicity by treatment technique or extent of nodal irradiation. There was a trend toward lower rates of grade ≥2 pneumonitis among IMRT patients compared to 3DCRT patients (5.4% vs. 23.0%, p=0.065). Local control and overall survival were similar between cohorts.

Conclusions—Acute and sub-acute toxicities were similar for patients treated with IMRT and with 3DCRT ± ENI, with a non-significant trend toward a reduction in pneumonitis with IMRT. Larger studies are needed to better define which patients will benefit from IMRT.

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Keywords

elective nodal irradiation; IMRT; esophagitis; pneumonitis; non-small cell lung cancer

Introduction

Definitive chemoradiation (CRT) is the standard-of-care for medically fit patients with unresectable stage III non-small cell lung cancer (NSCLC). Over the past two decades, radiotherapy techniques for lung cancer have gradually incorporated advancements in both imaging and radiation delivery, with a shift from two-dimensional simulation to computed tomography (CT)-based planning and more frequent incorporation of inverse planning with intensity-modulated radiation therapy (IMRT). Over the past decade, IMRT has been increasingly used in this setting despite a relative paucity of data demonstrating clinical benefits. IMRT is perceived to offer dosimetric advantages with the potential for dose escalation while sparing organs at risk such as the esophagus, heart, and spinal cord. Planning studies have suggested that IMRT can decrease dose to the esophagus and lung [1–3]. Theoretical concerns with IMRT have been raised regarding the possibility of variation in target dose delivery secondary to movement of the tumor and multi-leaf collimator,[4] although retrospective studies have suggested similar rates of disease control and survival for IMRT compared to 3D conformal radiation therapy (3DCRT).[5–7]

Pneumonitis is a serious and occasionally life-threatening complication following definitive CRT for locally advanced NSCLC, typically occurring several weeks to months after treatment. Acute esophagitis, while a common toxicity, is temporary and rarely results in percutaneous endoscopic gastrostomy (PEG) utilization or hospitalization, although opioid pain medications are frequently required. The role of IMRT in potentially decreasing acute or late toxicity has yet to be clearly defined. Studies comparing rates of toxicity between IMRT and 3DCRT have shown conflicting results. Some have suggested lower rates of severe pneumonitis [6, 8] and decreased rate of tube-feeding requirement with IMRT [9]. However, two population-based studies showed no difference in pulmonary, esophageal, or cardiac toxicities.[5, 7] A gradual reduction in the use of elective mediastinal nodal irradiation (ENI) in recent years [10, 11] also complicates and potentially confounds several of these retrospective analyses, particularly population-based studies. The present study evaluates a large series of patients treated with concurrent CRT for locally advanced NSCLC using one of three approaches: IMRT without ENI, 3DCRT without ENI, and 3DCRT with ENI, and compares acute toxicities, treatment-related hospitalizations, and oncologic outcomes between the 3 cohorts.

Methods and Materials

Patient Selection

Following Institutional Review Board approval, a retrospective review was performed on 153 consecutive patients with histologically-confirmed stage III NSCLC treated with definitive CRT between April 1994 and July 2014 at the University of California, Davis Cancer Center. Eight patients without on-treatment notes or available follow-up were

excluded, leaving 145 evaluable patients. Treatment planning approach (IMRT or 3DCRT) and use of ENI for each patient was documented. ENI was defined as coverage of clinically and pathologically uninvolved mediastinal and/or hilar nodal stations, and typically included coverage of the ipsilateral hilar, ipsilateral paratracheal (level 3P/4), and subcarinal nodes. Uninvolved supraclavicular and contralateral hilar nodes were not typically covered. One hundred and fifteen patients (79.3%) underwent staging with combined positron emission tomography (PET) and CT, and all others were staged with chest, abdomen and pelvis CT and magnetic resonance imaging or CT of the brain. Radiation technique was selected at treating physician discretion, but chronologically, IMRT was used increasingly over the study period with all IMRT patients treated after March 2009.

Radiation Therapy

Patients were immobilized in the supine position with a wingboard and/or custom vacuum lock cushion with arms above the head, and planning CT scans were obtained at 3 mm slice thickness with intravenous contrast used at treating physician discretion. Starting in January 2011, four-dimensional (4D)-CT simulation was incorporated. The gross tumor volume (GTV) was defined as primary tumor and involved lymph nodes identified by CT and PET scans, or pathologically via bronchoscopy or mediastinoscopy. Among 3DCRT patients, one of two approaches to lymph node treatment was used: involved field radiotherapy (IFRT), in which only gross nodal disease was targeted, and elective nodal irradiation (ENI), which prophylactically targeted uninvolved mediastinal nodal regions using a shrinking field technique, with opposed anterior/posterior fields covering the primary tumor and elective mediastinal nodes, followed by cone-down fields angled off the spinal cord to gross disease with margin. The elective nodal target typically included coverage of the ipsilateral hilar, ipsilateral paratracheal (level 3P/4), and subcarinal nodes with a 10–20 mm block edge margin, and the boost volume consisted of gross disease with a 15–20 mm block edge margin. For patients simulated with 4DCT, the internal target volume (ITV) was created using the maximal intensity projection and/or the maximal inhale/exhale phases. The clinical target volume (CTV) was defined by a 5–10 mm expansion on the GTV or ITV, and an additional planning target volume (PTV) margin of 5–12 mm was used. IMRT plans were designed with either static modulated coplanar fields (n= 28), volume modulated arcs (n=7), or helical tomotherapy (n=2). Among plans designed with static modulated fields, the median number of fields was 7 (range: 4–12 fields). One patient, classified as IMRT, was a treated with a hybrid plan with the first 10 fractions delivered with 3D conformal treatment and the remaining 20 delivered with an IMRT plan. Typical IMRT lung planning goals included a V20<35%, a mean lung dose<20 Gy, and a lung V5<65–70%, although patients were still treated at physician discretion when these constraints could not be achieved. No IMRT patient was treated with ENI. Treatment planning for all patients was completed using commercial planning software (Pinnacle; Philips Medical Systems, Andover, MA or Tomotherapy; Accuray, Sunnyvale, CA).

Radiation was delivered using megavoltage equipment with 6 MV or 18 MV photon beams to a median prescription dose of 61 Gy (range: 54–67 Gy) in 1.8–2.0 Gy daily fractions. IMRT patients underwent daily volumetric imaging with cone beam CT to assess alignment, and non-IMRT patients underwent weekly orthogonal portal imaging. During treatment,

patients were evaluated for acute toxicity at least weekly by an attending radiation oncologist. Follow-up CT scans were at the discretion of the treating physician, but were generally obtained at 3–4 month intervals for at least the first 2 years following completion of treatment. Routine post-treatment surveillance PET was not performed.

Dose volume histograms (DVH) were retrieved and reviewed for dosimetric variables, including PTV and GTV in cubic centimeters (cc), mean lung dose, percent whole-lung volume minus the CTV receiving at least 20 Gy (V20), and mean dose to the esophagus and heart. For 3DCRT-ENI patients, the volume of the boost PTV was documented rather than the elective nodal PTV, as the elective volumes were often drawn based on anatomic landmarks rather than volumetric contouring of all nodal regions at-risk. Twenty-four patients had no available dosimetric data, and cardiac and esophageal dose could not be retrieved or recreated for 66 (45.5%) and 86 (59.3%) patients, respectively.

Chemotherapy

All patients received concurrent systemic therapy. Sixty-one (42.1%) patients received carboplatin-based therapy in combination with paclitaxel or etoposide, 63 (43.4%) received cisplatin-based therapy, 5 (3.4%) received paclitaxel alone, 2 (1.4%) received carboplatin alone, 2 (1.4%) received cetuximab alone, and 1 (0.7%) received taxotere alone. Chemotherapy agent was unknown for 11 (7.6%) patients. Nine (6.2%) patients also received induction chemotherapy with carboplatin and paclitaxel (n=7), cisplatin and docetaxel (n=1), or cisplatin and paclitaxel (n=1). Seventy-seven patients (56%) received adjuvant systemic therapy and information on use of adjuvant systemic therapy was unavailable for 8 (5.5%).

Statistics

All statistical tests were performed using SPSS Version 22. Baseline characteristics and dosimetric variables among 3 groups consisting of patients treated with IMRT, 3DCRT-IFRT, or 3DCRT-ENI were compared using the one-way ANOVA for continuous variables (age, Karnofsky Performance Status (KPS) at baseline) and the chi-square test for categorical variables (gender, stage group, use of staging PET).

Esophagitis and pneumonitis were graded according to the Common Terminology Criteria for Adverse Events v4.0. Acute hospitalization was defined as hospital admission occurring during or within 3 months of completion of radiation treatment. Opioid use was defined as the requirement for opioids to relieve esophagitis-related pain during radiation treatment. Weight loss during treatment was analyzed by percentage decrease from weight at time of radiation oncology consultation to end of radiation treatment. Comparison of acute toxicities by treatment technique (IMRT vs. 3DCRT) and extent of nodal irradiation (3DCRT-IFRT vs. 3DCRT-ENI) was performed with Fisher’s exact test for categorical outcomes and with the independent samples t-test for continuous outcomes.

Oncologic endpoints included overall survival (OS), disease-free survival (DFS), locoregional control (LRC), and distant failure (DF). Disease-free survival was defined as time to recurrence or death from any cause. Locoregional failure was defined as recurrence within the ipsilateral lung, pleura, mediastinum, or regional nodes. Distant failure was

defined as biopsy-proven malignant pleural effusion or failure anywhere outside of a locoregional site, including contralateral lung recurrence. Survival analyses were performed using the Kaplan-Meier method and were compared between cohorts with the log-rank method. Patients without radiographic follow-up were excluded from failure analyses. Patients were censured at date of last follow-up for LRC, DF, and DFS analyses and at date of death or last follow-up, whichever was latest, for OS analysis. Potential prognostic variables included patient characteristics (age, gender, KPS, smoking pack-years), disease characteristics (histology, T and N stage, stage grouping), radiation treatment technique (IMRT vs. 3DCRT), extent of nodal irradiation, and treatment characteristics (radiation dose, chemotherapy agent). A p-value of ≤0.05 was considered statistically significant. Univariate analysis was performed to identify potential factors affecting failure and survival using the log-rank test for categorical variables and the Cox proportional hazards model for continuous variables. Prognostic factors significant on univariate analysis were included in step-wise multivariate analysis using the Cox proportional hazards regression model.

Results

Baseline Patient Characteristics

A total of 145 patients were analyzed, including 65 (44.8%) treated with 3DCRT-ENI, 43 (30.0%) with 3DCRT-IFRT, and 37 (25.5%) with IMRT. Baseline patient characteristics are summarized in Table 1. Among patients treated with IMRT, 3DCRT-IFRT, and 3DCRT-ENI, there was no significant difference in gender, KPS, or stage group (IIIA vs. IIIB). However, IMRT patients tended to be older than both cohorts of 3DCRT patients (median age 68 vs. 63 years, p=0.002). Use of staging PET-CT was significantly higher among IMRT (n=37, 100%) and 3DCRT-IFRT patients (n=38, 88.4%) compared to 3DCRT-ENI patients (n=40, 61.5%) (p<0.001).

Measures of Acute Toxicity

Table 2 summarizes acute and sub-acute toxicities for each treatment technique. We identified no significant difference in percent weight loss during treatment, incidence of acute hospitalization, grade ≥2 esophagitis or pneumonitis, or PEG utilization between 3DCRT and IMRT patients, and between 3DCRT-IFRT and 3DCRT-ENI patients. We identified a trend approaching significance for reduced incidence of grade ≥2 pneumonitis in IMRT patients as compared to 3DCRT patients as a group (5.4% vs. 23.0%, p=0.065), and when exploring the difference between those treated with and without ENI, IMRT patients had a significantly lower rate of pneumonitis compared to 3DCRT-ENI patients (p=0.03) but did not differ in pneumonitis rate with 3DCRT-IFRT patients (p=0.44).

Treatment Outcomes: Failure and Survival

The median time to last clinical follow-up was 9.5 months (range: 0.0–104.3), and the median time to last follow-up or death was 13.1 months (range: 0–104.3). Follow-up imaging was available for 138 (95.2%) patients. Actuarial 6-month, 1-year, and 2-year LRC rates were 76.5%, 65.8%, and 57.1%, respectively. There were no significant differences in local control by primary histology, stage grouping, treatment technique (IMRT vs. 3DCRT), or extent of nodal irradiation (3DCRT-IFRT vs. 3DCRT-ENI). Acute hospitalization was

associated with decreased LRC on univariate analysis, with an actuarial 1-year LRC of 55.8% vs. 69.8% (p=0.04).

Median time to DF was 14.4 months with a 1-year actuarial DF of 47.3%. Median DFS was 9.3 months. Median OS was 16.9 months, and actuarial 6-month, 1-year, 2-year, and 5-year OS were 64.1%, 45.2%, 32.1%, and 15.1%, respectively. Male gender (p=0.03), acute hospitalization (p=0.01), and increasing age (p=0.05) were associated with decreased OS on univariate and multivariate analyses.

Dosimetric Comparisons

The median PTV (using the boost PTV volume for 3DCRT-ENI plans) for all patients was 461.1 cc (range: 63.5–1404.7), with a smaller median PTV for the ENI group (406.0 cc; range: 63.5–628.1) compared to the IMRT group (515 cc; range: 170–1182) (p=0.02) and a trend toward reduced volume compared to the IFRT group (433 cc; range: 137–1405) (p=0.06). 3DCRT-ENI plans were dosimetrically inferior, with a higher mean cardiac dose compared to IMRT (p=0.007) and a trend toward higher cardiac dose compared to 3D-IFRT (p=0.08). 3DCRT-ENI also resulted in a higher maximum spinal cord dose compared to both 3DCRT-IFRT (p=0.0003) and IMRT (p<0.0001). Mean lung dose and lung V20 did not differ significantly between the 3 groups, and there were no statistically significant dosimetric differences between 3DCRT-IFRT and IMRT for lung, heart, spinal cord, or esophageal dose. Dosimetric data is outlined in Table 3.

Discussion

IMRT has been increasingly used for the treatment of stage III NSCLC in recent years despite a lack of robust clinical evidence supporting its use in this setting, largely due to perceived dosimetric advantages. Theoretical concerns with IMRT have been raised regarding the possibility of compromised oncologic outcomes: the higher conformality of IMRT may predispose to more out-of-field failures, and movement of the tumor and multi-leaf collimator may lead to variation in target dose delivery.[4, 7, 12–14] In the present series, radiation technique and use of ENI did not predict for LRC, DF, OS, or DFS, consistent with other reports,[5] although a series from a single institution suggested a survival benefit with IMRT.[6] Our results confirm that IMRT offers similar oncologic and survival outcomes compared to 3DCRT in the setting of definitive chemoradiation for stage III NSCLC.

IMRT may improve esophageal dosimetric parameters via increased dose conformity to the target volumes, although the role of IMRT in clinically decreasing acute esophageal toxicity is inconsistent among existing studies. In the present series, we performed an exploratory dosimetric comparison between the 3 approaches that was unfortunately limited by the availability of DVH data for a subset of older plans. We demonstrated the expected reductions in heart and spinal cord dose with the omission of ENI, but did not clearly identify dosimetric differences between 3DCRT-IFRT and IMRT. The analysis was likely underpowered to identify small differences. The median PTV size was larger among IMRT patients, likely reflecting selection bias for use of IMRT for larger or more advanced tumors and suggesting IMRT may allow safe delivery of thoracic radiotherapy for patients with

larger target volumes, although the size difference between IMRT and 3DCRT-IFRT did not reach statistical significance. More nuanced comparisons between patients with similar target volumes, similar lung V20, or both could provide valuable additional information on potential benefits of IMRT, but our dataset with full dosimetric information was too small for these analyses.

A recently reported exploratory, non-randomized analysis from Radiation Therapy Oncology Group (RTOG) 0617 comparing IMRT and 3DCRT demonstrated significantly less decline in patient-reported quality of life (QOL) with IMRT up to 1 year from treatment.[15] However, associated esophageal and lung toxicities that may lead to QOL declines were not reported between radiation techniques. A better understanding of the cause of this difference in QOL is desirable to allow further refinements in treatment technique. Sub-group analyses from RTOG 0617 also identified increasing cardiac volume receiving 5 Gy (V5) or 30 Gy (V30) as an independent predictors of decreased overall survival on multivariate analysis. Radiotherapy technique (IMRT vs. 3DCRT) was not a significant predictor of overall survival in this analysis; however, the cardiac constraints mandated by the protocol were relatively liberal [16]. The results suggest cardiac dose may be an important predictor of survival, and that future trials should incorporate more rigorous cardiac dose/volume goals. Ultimately, reduced cardiac dose could prove an important benefit of IMRT for well-selected patients. We were unable to include a comparison of cardiac toxicity in the present study due to a lack of available cardiac follow-up data and a relatively modest median follow-up period.

Our results are similar to those of two recent Surveillance, Epidemiology, and End Results (SEER)-Medicare analyses demonstrating similar lung and esophageal toxicity for IMRT and 3DCRT.[5] As Harris *et al* discuss, registry-based analyses are limited by the inability to identify patients undergoing ENI, the use of which may vary by technique. By contrast, studies from the University of Texas M. D. Anderson Cancer Center have identified lower rates of pneumonitis following treatment with IMRT. In a retrospective review comparing the incidence of treatment-related pneumonitis between 151 NSCLC patients treated with concurrent chemotherapy and IMRT and 222 similar patients treated with 3DCRT, Yom *et al* identified rates of grade ≥3 pneumonitis at 12 months of 8% for IMRT vs. 32% for 3DCRT (p=0.002).[9] These results were confirmed in a follow-up study with larger patient numbers and longer follow-up.[6] The present study similarly demonstrated a trend toward reduced pneumonitis with IMRT.

Interestingly, a recent series investigating outcomes in patients with small cell lung cancer treated with IMRT or 3DCRT demonstrated significantly lower rates of PEG requirement with IMRT vs. 3D (5 vs. 17%).[6] By contrast, our rates of PEG requirement were similar between the two groups and much lower at <3% (Table 2), likely because small cell lung cancer more frequently presents in a central location which may translate into higher esophageal doses.

As with other published series evaluating IMRT in NSCLC patients, our study is limited by the inherent bias of a retrospective study design and the potential for uncontrolled confounding factors. Due to the long time span of our study, we were unable to retrieve all

treatment plans and had only limited dosimetric data available for an exploratory analysis. The possibility of increased use of IMRT with anatomically complex cases, such as cases with contralateral mediastinal or supraclavicular nodal involvement, could potentially have obscured significant differences in toxicity favoring IMRT. Other technical factors have also evolved over the study period and were not fully controlled for, including increased use of simulation with 4DCT and enhanced image guidance with cone beam CT for IMRT patients. A lack of homogeneity in choice of CTV and PTV margins used over the study period was also a potentially a confounding factor. Large target volume margins could potentially deliver dose to a large swath of elective nodes unintentionally. The IMRT patients in our cohort had a higher median age than 3DCRT patients, although there was no significant difference in KPS, suggesting increasing comfort with treating elderly patients with good performance status in recent years. However, elderly patients may be predisposed to more severe acute toxicity secondary to comorbid conditions and decreased reserve in multiple organs, which may theoretically have diminished our ability to detect significant improvements in toxicity outcomes among IMRT patients. With 145 patients, our study may have been underpowered to detect subtle differences in dosimetric, toxicity or oncologic outcomes. Nonetheless, given the very limited published clinical outcomes data evaluating IMRT for locally advanced lung cancer, our series adds to the available literature on this topic and suggests further prospective data is warranted to justify the increased costs of routine IMRT for locally advanced NSCLC cases.

In aggregate, the available data supporting the use of IMRT for locally advanced lung cancer is limited and does not clearly demonstrate consistent, clinically meaningful reductions in toxicity. The non-randomized QOL data from RTOG 0617 remain the most robust evidence in support of routine use of IMRT in this setting. The available single-institution and registry-based studies report conflicting findings. In the present study, we found no evidence that IMRT reduces such clinically meaningful parameters as PEG placement, opioid analgesia requirement, weight loss during treatment, or hospitalization. Although not reaching statistical significance, our data do lend support to a possible modest reduction in pneumonitis following IMRT in agreement with other published retrospective series, a trend that requires further, preferably prospective data, as validation. Dosimetrically, IMRT was superior to 3DCRT-ENI, but not clearly superior to 3DCRT-IFRT.

Conclusions

Rates of esophagitis, PEG placement, opioid analgesia, hospitalization, and weight loss on treatment were similar with IMRT and 3DCRT, with or without use of ENI. We identified a trend consistent with some prior retrospective data suggesting that IMRT may be associated with lower rates of pneumonitis compared with 3DCRT, and IMRT may allow treatment of larger target volumes without excess toxicity. Our study further suggests that IMRT offers similar disease outcomes and rates of acute toxicity compared to 3DCRT in the treatment of stage III NSCLC.

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Clinical Practice Points

Definitive CRT is the standard-of-care for medically fit patients with unresectable stage III NSCLC. Over the past decade, IMRT has been increasingly used in this setting despite a relative paucity of data demonstrating clinical benefits. IMRT is perceived to offer dosimetric advantages with the potential for dose escalation while sparing organs at risk such as the esophagus, heart, and spinal cord. However, the role of IMRT in potentially decreasing acute or late toxicity has yet to be clearly defined, with theoretical concerns regarding potentially increased risk of pneumonitis secondary to low dose wash to surrounding normal lung parenchyma. Studies comparing rates of toxicities between IMRT and 3DCRT have shown conflicting results.

We found that rates of esophagitis, PEG placement, opioid analgesia requirement, hospitalization, and weight loss on treatment were similar between IMRT and 3DCRT with or without use of ENI. We identified a trend consistent with some prior retrospective studies suggesting that IMRT may be associated with lower rates of pneumonitis compared with 3DCRT. Local control and overall survival were similar between cohorts. Our data suggest that IMRT may allow treatment of larger target volumes without excess toxicity and without compromising disease control or survival, but analyses of larger datasets are needed to better define which patients will benefit from IMRT.

Table 1

Baseline Patient Characteristics

Characteristic	Value (% or range)
Median age	64 (41–90)
Male	91 (62.8%)
Median KPS	80 (60–100)
Median smoking history in pack-years	40 (0–175)
Histology	
Adenocarcinoma	55 (37.9%)
Squamous cell carcinoma	47 (32.4%)
NSCLC not otherwise specified	38 (26.2%)
Large cell/Neuroendocrine	2 (1.4%)
Other*	3 (2.1%)
Stage	
IIIA	89 (61.4%)
IIIB	56 (38.6%)

Abbreviations: KPS = Karnofsky Performance Status; NSCLC = non-small cell lung cancer.

*Other = 1 adenosquamous/mucoepidermoid, 1 mixed adenocarcinoma and squamous cell carcinoma, and 1 broncheoalveolar carcinoma.

Table 2

Measures of Acute Toxicity By Treatment Technique

	N (%)					
	Grade ≥2 Esophagitis	**Grade ≥2 Pneumonitis**	**PEG utilization**	**Narcotics**	**Hospitalization**	**Median Percent Weight Loss**
3D-ENI	18 (27.7%)	15 (23.1%)	1 (1.5%)	23 (35.4%)	26 (40.0%)	−2.93%
3D-IFRT	9 (20.9%)	5 (11.6%)	1 (2.3%)	9 (20.9%)	13 (30.2%)	−3.87%
IMRT	8 (21.6%)	2 (5.4%)	1 (2.7%)	14 (37.8%)	9 (24.3%)	−3.88%
All	35 (24.1%)	22 (15.2%)	3 (2.1%)	46 (31.7%)	48 (33.1%)	−3.63%

Abbreviation s: ENI = elective nodal irradiation; IFR T = involved field radiotherapy; IMRT = intensity-modula ted radiation therapy; PEG = percutaneous endoscopic gastrostomy

Table 3

Dosimetric comparison by treatment technique

	Median (range)					
	PTV (cc)	**Mean lung dose (Gy)**	**Lung V20 (%)**	**Mean cardiac dose (Gy)**	**Mean esophageal dose (Gy)**	**Spinal cord maximum (Gy)**
3D-ENI	406 (64–628)	16.6 (9.8–22.9)	29 (15–48)	16.2 (3.8–39.9)	* NA	47.2 (19.2–58.2)
3D-IFRT	433 (137–1405)	15.1 (8.1–22.7)	26 (13–47)	13.4 (0.7–36.3)	27.7 (3.4–53.5)	43.9 (15.0–48.6)
IMRT	515 (170–1182)	16.5 (5.6–20.7)	30 (13–38)	8.6 (0.16–32.3)	26.1 (6.1–51.3)	43.2 (13.3–50.7)

* Insufficient patients treated with 3D-ENI had available esophageal dose metrics for analysis

Abbreviations: ENI = elective nodal irradiation; IFRT = involved field radiotherapy; IMRT = intensity-modulated radiation therapy; PTV: Planning target volume; V20: percent receiving 20 Gy