Published in final edited form as:

Radiother Oncol. 2016 October ; 121(1): 70–74. doi:10.1016/j.radonc.2016.08.005.

Bayesian regression analyses of radiation modality effects on pericardial and pleural effusion and survival in esophageal cancer

Liru He^{a,1}, Andrew Chapple^{b,1}, Zhongxing Liao^d, Ritsuko Komaki^d, Peter F. Thall^{c,*}, and Steven H. Lin^{d,*}

^aDepartment of Radiation Oncology, Sun Yat-Sun University Cancer Center, Collaborative Innovation Center for Cancer Medicine, Guangzhou, China

^bDepartment of Statistics, Rice University, Houston Texas, USA

^cDepartment of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA

^dDepartment of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA

Abstract

Background and Purpose—To evaluate radiation modality effects on pericardial effusion (PCE), pleural effusion (PE) and survival in esophageal cancer (EC) patients.

Materials and Methods—We analyzed data from 470 EC patients treated with definitive concurrent chemoradiotherapy (CRT). Bayesian semi-competing risks (SCR) regression models were fit to assess effects of radiation modality and prognostic covariates on the risks of PCE and PE, and death either with or without these preceding events. Bayesian piecewise exponential regression models were fit for overall survival, the time to PCE or death, and the time to PE or death. All models included propensity score as a covariate to correct for potential selection bias.

Results—Median times to onset of PCE and PE after RT were 7.1 and 6.1 months for IMRT, and 6.5 and 5.4 months for 3DCRT, respectively. Compared to 3DCRT, the IMRT group had significantly lower risks of PE, PCE, and death. The respective probabilities of a patient being alive without either PCE or PE at 3-years and 5-years were 0.29 and 0.21 for IMRT compared to 0.13 and 0.08 for 3DCRT. In the SCR regression analyses, IMRT was associated with significantly lower risks of PCE (HR=0.26) and PE (HR=0.49), and greater overall survival (probability of beneficial effect (*pbe*) > 0.99), after controlling for known clinical prognostic factors.

Corresponding authors: Steven H. Lin, M.D., Ph.D., Department of Radiation Oncology, Unit 0097, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030, USA Telephone (713) 563-2305; FAX (713) 563-2331; shlin@mdanderson.org, Peter F. Thall, Ph.D., The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030, USA; (713) 794-4162; rex@mdanderson.org.

¹These authors contributed equally to the work

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Conclusions—IMRT reduces the incidence and postpones the onset of PCE and PE, and increases survival probability, compared to 3DCRT.

Keywords

Esophageal carcinoma; Radiation; Pericardial effusion; Pleural effusion; Survival; Propensity score

Esophageal cancer (EC) is the eighth most common cancer worldwide [1]. For patients with unresectable disease, definitive concurrent chemoradiotherapy (CRT) has been established as the standard treatment. While survival has significantly increased over the years with advances in treatment delivery and surgical techniques, late onset toxicities of CRT such as cardiopulmonary events are common adverse effects. Among these, pericardial effusion (PCE) and pleural effusion (PE) are two of the most frequency events [2,3,4].

Although previous studies have reported late-onset adverse events associated with the treatment of EC [2–8], sample sizes of those studies often were small, and older radiation techniques were evaluated (two-dimensional RT (2DRT) or three-dimensional conformal radiation therapy RT (3DCRT)). Radiation modalities such as intensity-modulated radiation therapy (IMRT) can deliver more conformal treatments and potentially can result in fewer treatment-related toxicities [9–12]. However, to the best of our knowledge, reports of the incidence, severities, and related factors of PCE and PE using IMRT compared with 3DCRT have not been reported. Another limitation of these earlier studies is that they often define failures as death or effusion, which greatly simplify the problem, since it throws away most of the information of the semi-competing risk nature of “death”, which effectively censors the development of any effusion, and “effusion”, which doesn’t censor death.

In this study, we retrospectively evaluated the incidence and severity of PCE and PE, and survival time, after definitive CRT in a cohort of 470 EC patients treated with either IMRT or 3DCRT, while accounting for effects of established prognostic risk factors and the semi-competing risk nature of death and the development of effusion.

Materials and Methods

Patient selection

This study was performed in accordance with the Declaration of Helsinki and was approved by the institutional review board of a NCI-designated comprehensive cancer center. We retrospectively reviewed medical and radiation records of all EC patients treated with definitive CRT between January 1998 and April 2012 at our institution. Criteria for inclusion in our study were as follows: pathologically confirmed primary EC, treated with 3DCRT or IMRT modality, availability of dose–volume histograms (DVHs) for the heart and lungs, availability of radiographic images and adequate follow-up records to assess clinical symptoms. Exclusion criteria were treatment involving thoracic surgery, previous chest RT, malignant or infectious pleural effusion and unknown critical clinical information.

Treatment approaches

Simulation CT was performed with 5-mm slices in supine position under normal quiet breathing condition. The heart surface and total lungs were delineated manually on each axial CT slice. Heart was defined from the inferior border of the right pulmonary artery through to the apex of the heart. Total lungs were delineated excluding the bronchus. The clinical target volume (CTV) included the gross primary tumor volume (GTV) with a radial margin of 0.5–1 cm and a proximal and distal margin of 3–4 cm, and also covered the elective nodal regions. The nodal CTV was defined by a 0.5–1 cm expansion around the nodal GTV. The planning target volume (PTV) was the CTV plus a uniform margin of 1.0-cm expansion for 3DCRT and a 0.5-cm expansion margin for IMRT. The typical radiation dose was 50.4 Gy in 28 fractions, once daily, 5 days a week. All patients received platin- and/or taxane-based chemotherapy with or without fluorouracil, given weekly during the radiotherapy. Image-guided setup for 3DCRT involved weekly MV portal imaging, where it involved daily KV orthogonal imaging for IMRT setup.

Clinical evaluation and follow-up

During therapy, symptoms were closely monitored on a weekly basis. After completing CRT, patients have a short follow up with repeat esophagogastroduodenoscopy (EGD) and FDG-PET-computed tomography (CT) imaging for restaging purposes and surgical evaluation. After completing all treatments, patients were generally followed up every 3–4 months for the first 3 years and every 6–12 months thereafter. PCE and PE were assessed from the follow-up chest CT scans and/or X-rays, and were graded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0. Recurrent PCE/PE was defined when the PCE/PE recurred after the first PCE/PE had been totally absorbed.

Statistical methods

Associations between RT modality and categorical or continuous covariates were evaluated by Fisher exact tests or Kruskal-Wallis tests, respectively. Because patients were not randomized between IMRT and 3DCRT, to correct for potential bias overall unadjusted event time distributions were estimated using inverse probability of treatment weighted (IPTW) Kaplan-Meier plots and compared between groups by IPTW adjusted log rank tests [13,14]. Bayesian piecewise exponential regression models were fit for overall survival, the time to PCE or death, and the time to PE or death. Because death and effusion are semi-competing risks (SCRs), there were three different transition times: (1) RT to effusion, (2) RT to death without effusion, and (3) death following effusion. The SCR structure is illustrated by Fig. 1. For each type of effusion, the Bayesian SCR regression model of Lee et al. [15] was fit to assess effects of RT modality and prognostic covariates on the risks of the three events. Standard statistical computations were done in R studio Version 0.98.1062. The SCR models were fit using the computer program provided by Lee et al. [15], and are given in Supplementary Tables 3 and 4. 10-fold likelihood cross validation was used to select the covariates used in the regression models. Propensity score was included as a covariate in each linear term of each regression model to correct for bias due to non-randomization. To interpret the fitted regression Bayesian models, for each covariate and each transition event,

PHE = posterior probability of a harmful effect. Equivalently, $PBE = 1 - PHE$ = posterior probability of a beneficial effect. Values of PHE or PBE either .95 or .05 may be considered significant, and values .99 or .01 may be considered highly significant.

Results

Patient Characteristics

The median follow up time was 14.0 months for 3DCRT group, and 20.2 months for IMRT group, respectively. Patients' characteristics are summarized in Table 1. IMRT patients were slightly younger, but were more likely to present with hypertension compared with 3DCRT patients.

Unadjusted analyses of effusion and death

From the final date of radiation, 94 patients experienced PCE and 71 (75.5%) subsequently died, while the remaining 285 patients died without PCE; 187 patients experienced PE and 159 (85.0%) subsequently died, while the remaining 197 patients died without PE (Fig. 1). The rates of recurrent PCE (1.2% vs. 9.0%, $P < 0.001$) and PE (5.8% vs. 11.8%, $P = 0.030$) were significantly lower in the IMRT group than in the 3DCRT group (Supplementary Table 2).

As it shown in Table 2, IMRT had much larger median, 3-, and 5-year survival, compared to 3DCRT. IMRT was similarly superior to 3DCRT in terms of time to death or PE, time to death or PCE, and time to death or either type of effusion. Corresponding IPTW adjusted KM plots for each modality and failure time are given in Fig. 2. The median time to PCE or death was 18.7 months for IMRT versus 7.8 months for 3DCRT, and the 3- and 5-year survival probability were 37.5% and 27.0% for IMRT, and 19.9% and 11.6% for 3DCRT, respectively ($P < 0.001$). While the median time to PE or death was 15.4 months for IMRT versus 6.7 months for 3DCRT, and the 3- and 5-year survival probability were 32.0% and 24.3% for IMRT, and 17.6% and 11.9% for 3DCRT, respectively ($P < 0.001$).

Bayesian regression analyses of effusion and death

Fitted Bayesian piecewise exponential regression models are summarized for overall survival (Table 3), the time to PE or death and the time to PCE or death (Table 4). All models included an RT modality indicator, two indicators for type of concurrent chemo, whether induction chemo was given, and propensity score to correct for bias due to the fact that patients were not randomized, type of chemo. The remaining seven covariates were chosen from an initial set of 11 using 10-fold likelihood cross-validation, described in the Supplementary materials. All three fitted models showed that after adjusting for effects of prognostic covariates and other treatment variables, the posterior probability that IMRT was beneficial compared to 3D-CRT was > 0.99 .

Bayesian semi-competing risks regression analyses of effusion and death

In the SCR model based analyses, IMRT patients had significantly lower hazards of PCE ($HR = 0.26$, $PBE > 0.99$) and death without PCE ($HR = 0.47$, $PBE > 0.99$), compared to 3DCRT patients (Supplementary Table 3). The risk of PE ($HR = 0.49$, $PBE > 0.99$) and death

without PE (HR=0.49, $P_{BE} > 0.99$) were also lower for IMRT patients compared to those for 3DCRT patients (Supplementary Table 4).

Comparison of DVH parameters between groups

The following comparisons were done for the cohort of 345 patients with DVH values (Supplementary Table 5). The mean heart dose and mean lung dose were 22.4 Gy and 10.9 Gy for IMRT versus 31.4 Gy and 12.8 Gy for 3DCRT ($P < 0.001$), respectively. IMRT patients have significantly lower V30 (0.32 vs. 0.60, $P < 0.001$), V40 (0.19 vs. 0.45, $P < 0.001$) and V50 (0.08 vs. 0.19, $P < 0.001$) of the heart than 3DCRT patients. The V5 (0.50 vs. 0.55, $P = 0.006$) and V10 (0.34 vs. 0.41, $P < 0.001$) of the lung were significantly lower for IMRT group than those for 3DCRT group but no differences were seen for V15 and V20 (Supplementary Table 5).

Discussion

IMRT has been shown to reduce radiation dose to adjacent organs compared to 3DCRT in numerous dosimetric studies [11,12,7,8], but how this translates to clinical benefit for esophageal cancer patients, especially the risk of developing PCE and PE, is largely unknown. In the present study, our results showed that IMRT decreased the incidence and postponed the median onset time of PCE and PE, and increased the survival probability of PCE or death and PE or death compared to 3DCRT.

Several previous studies have reported the onset patterns of PCE and PE with 3DCRT and dosimetric predictors of these toxicities. Wei et al reported a PCE incidence of 27.7% with a prescription dose of 45–50.4 Gy, and the median onset time was 5.3 months [8]. Fukada et al reported an even higher PCE incidence of 35.9% with a prescription dose of 60 Gy by the techniques of 2D and 3DCRT, and the median onset time was 6 months [5]. Our PCE results for 3DCRT (28.3%, 6.5 months) were comparable with the previous studies, but for IMRT, the incidence was much lower (13.2%), and the median onset time was also longer (7.1 months). These data, taken together, suggest that IMRT decreases the incidence and postpones the onset time of PCE compared to 3DCRT. When it comes to the onset pattern of PE, previous studies mainly focused on symptomatic PE (grade 2), with a reported incidence of 9%–19% using 2D or 3DCRT [3,4,9]. In our study, we observed an incidence of symptomatic PE of 7.1% with 3DCRT, compared to 3.1% for IMRT.

The most important finding of this study is that IMRT decreased the risks of PCE, PE, and death compared to 3DCRT, while accounting for effects of other clinically relevant covariates. One study that compared the long-term outcomes of EC patients after 3DCRT or IMRT indicated that 3DCRT patients had a significantly greater risk of non cancer-specific death compared to IMRT, while no difference was seen in cancer-specific mortality between the two groups [7]. Collectively, these data suggested that the survival benefit of IMRT could have resulted from the less toxic sequela of treatment compared to 3DCRT.

What accounts for the different incidences of these toxicities with the two modalities? We found that as a whole, IMRT patients had significantly lower median dose and nearly all V5–20 and V30–50 parameters for the lung and heart, respectively, than 3DCRT patients.

With regard to which DVH parameters that could predict the risk of PCE or PE, results from different groups vary considerably, and there is no consensus about which parameters are most reliable. For example, heart V30 and mean heart dose were individually reported to be associated significantly with PCE by Wei et al.[8] and Marks et al. [20]. But Hayashi et al [19] suggested that V10 of the heart as the most influential factor. For PE, Shirai et al. suggested heart V50 as a useful parameter for assessing the risk of PE but not any DVH parameters of the lung [7]. It is believed that PE after CRT may be associated with RT-induced heart damage, and the RT-induced PCE may also be related with the pathophysiology changes of the lung. So, instead of analyzing DVH parameters of the heart and lung separately as most of the previous studies, we included both heart and lung DVH parameters together with RT modality and PTV in our SCR model based analyses. Our fitted DVH SCR models showed that IMRT, and lung V10, were independent factors that predict lower risk of PCE, while higher PTV and lung V15 were associated with higher risks of PE and death without either type of effusion.

Our study is limited by the nature of a retrospective study, for the non-randomized comparison makes the analysis subject to potential selection biases. Since IMRT is a more advanced technology which was adopted later in time compared to 3DCRT, 3DCRT and IMRT patients were mostly treated in two different time periods. In order to minimize the potential biases, we have applied well-established statistical methods to adjust for imbalances that are inherent in observational datasets, in order to provide the best comparison between 3DCRT and IMRT based on the available data. We believe that possible substantive heterogeneities in the outcomes due to time differences were accounted for by the IPTW and propensity score methodologies.

In conclusion, we found IMRT decreased the incidence, postponed the median onset time of PCE and PE, and increased the survival probability of PCE or death and PE or death compared to 3DCRT. Accounting for effects of other clinically relevant covariates, IMRT was still an independent factor that significantly lowered the risks of PCE, PE, and death. Although these results need confirmation, IMRT should be the preferred technique for the treatment of esophageal cancer in order to minimize the development of treatment related toxicities such as PCE and PE.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work is financially supported by the National Cancer Institute Cancer Center Support Grant CA016672.

Conflict of interest statement:

SHL has research funding from Elekta, STCube Pharmaceuticals and Roche/Genentech, has received honorarium from AstraZeneca, US Oncology and ProCure.

References

1. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. *CA Cancer J Clin.* 2015; 65:87–108. [PubMed: 25651787]
2. Ishikura S, Nihei K, Ohtsu A, et al. Long-term toxicity after definitive chemoradiotherapy for squamous cell carcinoma of the thoracic esophagus. *J Clin Oncol.* 2003; 21:2697–702. [PubMed: 12860946]
3. Kumekawa Y, Kaneko K, Ito H, et al. Late toxicity in complete response cases after definitive chemoradiotherapy for esophageal squamous cell carcinoma. *J Gastroenterol.* 2006; 41:425–32. [PubMed: 16799883]
4. Morota M, Gomi K, Kozuka T, et al. Late toxicity after definitive concurrent chemoradiotherapy for thoracic esophageal carcinoma. *Int J Radiat Oncol Biol Phys.* 2009; 75:122–8. [PubMed: 19327900]
5. Fukada J, Shigematsu N, Takeuchi H, et al. Symptomatic pericardial effusion after chemoradiation therapy in esophageal cancer patients. *Int J Radiat Oncol Biol Phys.* 2013; 87:487–93. [PubMed: 23968770]
6. Konski A, Li T, Christensen M, et al. Symptomatic cardiac toxicity is predicted by dosimetric and patient factors rather than changes in 18F-FDG PET determination of myocardial activity after chemoradiotherapy for esophageal cancer. *Radiother Oncol.* 2012; 104:72–7. [PubMed: 22682539]
7. Shirai K, Tamaki Y, Kitamoto Y, et al. Dose-volume histogram parameters and clinical factors associated with pleural effusion after chemoradiotherapy in esophageal cancer patients. *Int J Radiat Oncol Biol Phys.* 2011; 80:1002–7. [PubMed: 20542385]
8. Wei X, Liu HH, Tucker SL, et al. Risk factors for pericardial effusion in inoperable esophageal cancer patients treated with definitive chemoradiation therapy. *Int J Radiat Oncol Biol Phys.* 2008; 70:707–14. [PubMed: 18191334]
9. Chandra A, Guerrero TM, Liu HH, et al. Feasibility of using intensity-modulated radiotherapy to improve lung sparing in treatment planning for distal esophageal cancer. *Radiother Oncol.* 2005; 77:247–53. [PubMed: 16298001]
10. Fenkell L, Kaminsky I, Breen S, et al. Dosimetric comparison of IMRT vs. 3D conformal radiotherapy in the treatment of cancer of the cervical esophagus. *Radiother Oncol.* 2008; 89:287–91. [PubMed: 18789828]
11. Nutting CM, Bedford JL, Cosgrove VP, et al. A comparison of conformal and intensity-modulated techniques for oesophageal radiotherapy. *Radiother Oncol.* 2001; 61:157–63. [PubMed: 11690681]
12. Wu VW, Sham JS, Kwong DL. Inverse planning in three-dimensional conformal and intensity-modulated radiotherapy of mid-thoracic oesophageal cancer. *Br J Radiol.* 2004; 77:568–72. [PubMed: 15238403]
13. Cole SR, Hernan MA. Adjusted survival curves with inverse probability weights. *Comput Methods Programs Biomed.* 2004; 75:45–49. [PubMed: 15158046]
14. Sugihara S. Survival analysis using inverse probability of treatment weighted methods based on the generalized propensity score. *Pharm Stat.* 2010; 9:21–34. [PubMed: 19199275]
15. Lee KH, Haneuse S, Schrag D, Dominici F. Bayesian semiparametric analysis of semicompeting risks data: investigating hospital readmission after a pancreatic cancer diagnosis. *J R Stat Soc Ser C Appl Stat.* 2015; 64:253–73.
16. Ibrahim JG, Chen M-H, Sinha D. *Bayesian Survival Analysis*, Springer Series in Statistics. 2001
17. Lin SH, Wang L, Myles B, et al. Propensity score-based comparison of long-term outcomes with 3-dimensional conformal radiotherapy vs intensity-modulated radiotherapy for esophageal cancer. *Int J Radiat Oncol Biol Phys.* 2012; 84:1078–85. [PubMed: 22867894]
18. Mayo CS, Urie MM, Fitzgerald TJ, et al. Hybrid imrt for treatment of cancers of the lung and esophagus. *Int J Radiat Oncol Biol Phys.* 2008; 71:1408–18. [PubMed: 18262730]
19. Hayashi K, Fujiwara Y, Nomura M, et al. Predictive factors for pericardial effusion identified by heart dose-volume histogram analysis in oesophageal cancer patients treated with chemoradiotherapy. *Br J Radiol.* 2015; 88:20140168. [PubMed: 25429644]
20. Marks LB, Yu X, Prosnitz RG, et al. The incidence and functional consequences of rt-associated cardiac perfusion defects. *Int J Radiat Oncol Biol Phys.* 2005; 63:214–23. [PubMed: 16111592]

Figure 1.

Frequency of the competing risk of effusion event or death after completing chemoradiotherapy. (A) Patients who developed pericardial effusion or death as the initial event or death after the development of pericardial effusion. (B) Patients who developed pleural effusion or death as the initial event or death after the development of pleural effusion.

Figure 2.

IPTW adjusted Kaplan-Meier survival curves. (A) IPTW adjusted Kaplan-Meier estimates of the time to death or pericardial effusion curves, along with 95% confidence intervals; (B) IPTW adjusted Kaplan-Meier estimates of the time to death or pleural effusion curves, along with 95% confidence intervals.

Table 1

Summary of patient covariates for the 3DCRT and IMRT treatment groups.

Variables	3DCRT (%)	IMRT (%)	Total (%)	P-value
No. of patients	212	258	470	
Age, median (range)	67.5 (30–87)	65 (20–89)	66 (20–89)	0.0328
Gender=Male	170 (80.2)	202 (78.3)	372 (79.1)	0.8914
Race=White	184 (86.8)	214 (82.9)	398 (84.7)	0.7469
Black	9 (4.2)	14 (5.4)	23 (4.9)	
Hispanic	12 (5.7)	19 (7.4)	31 (6.6)	
Asian	7 (3.3)	11 (4.3)	18 (3.8)	
BMI, median (range)	26.8 (15.2–53.8)	26.6 (15.2–64.9)	26.6 (15.2–64.9)	0.9231
KPS Score= Good	174 (82.1)	214 (82.9)	393 (83.6)	0.4532
Smoker=Yes	47 (22.2)	60 (23.2)	107 (22.8)	0.8254
Hypertension=Yes	103 (48.6)	157 (60.8)	260 (55.3)	<0.01
CABG History=Yes	17 (8.0)	25 (9.7)	42 (8.9)	0.6265
Diabetes=Yes	36 (17.0)	54 (20.9)	90 (19.1)	0.2914
Asthma=Yes	10 (4.7)	7 (2.7)	17 (3.6)	0.3219
Location=Upper	27 (12.7)	41 (15.9)	68 (14.5)	0.1373
Mid	14 (6.6)	28 (10.8)	42 (8.9)	
Distal	171 (80.7)	189 (73.3)	360 (76.6)	
Histology=Adeno	136 (64.1)	181 (70.1)	317 (67.4)	0.1984
Differentiation=Well	4 (1.9)	5 (1.9)	9 (1.9)	0.0698
Moderate	81 (38.2)	111 (43.1)	192 (40.8)	
Poor	122 (57.5)	142 (55.0)	264 (56.2)	
Unknown	5 (2.4)	0 (0)	5 (1.1)	
Stage=3 or 4	139 (65.6)	172 (66.7)	311 (66.2)	0.8448
Induction	76 (35.8)	77 (29.8)	153 (32.5)	0.1984
Chemo=Yes Dose, median (range)	50.4 (14.8–66)	50.4 (16.2–66)	(14.8–66)	0.2043

3DCRT= 3D conformal radiotherapy; IMRT= Intensity modulated radiation therapy; BMI= Body mass index; KPS=Karnofsky performance status; CABG=Coronary artery bypass graft; Adeno=adenocarcinoma.

Table 2
Summary statistics for unadjusted times to (1) death, (2) death or PE, (3) death or PCE, and (4) death or either PE or PCE.

	Overall Survival		Death or Pleural Effusion		Death or Pericardial Effusion		Death or Either Type of Effusion	
	3DCRT	IMRT	3DCRT	IMRT	3DCRT	IMRT	3DCRT	IMRT
Median (95% CI)	71.9 (57.3–83.4)	106.7 (84.6–131.3)	28.6 (24.1–33.0)	65.9 (55.1–78.9)	33.6 (30.0–3.6)	80.3 (70.7–91.9)	21.7 (20.6–24.7)	49.6 (40.7–63.0)
Pr[Time > 3 Years] (95% CI)	0.31 (0.27–0.36)	0.42 (0.38–0.47)	0.17 (0.14–0.21)	0.32 (0.27–0.36)	0.19 (0.16–0.23)	0.37 (0.33–0.42)	0.13 (0.10–0.16)	0.29 (0.25–0.33)
Pr[Time > 5 Years] (95% CI)	0.20 (0.16–0.24)	0.30 (0.25–0.35)	0.11 (0.09–0.15)	0.23 (0.19–0.29)	0.11 (0.08–0.14)	0.26 (0.22–0.31)	0.08 (0.05–0.10)	0.21 (0.17–0.26)

All *P*-values for 3DCRT-versus-IMTRT comparisons are < 0.01. *P* = Probability.

Table 3

Fitted Bayesian regression models for overall survival.

Variable	Posterior Quantities for Overall Survival	
	Median HR (95% CI)	PHE
IMRT	0.86 (0.77–0.96)	<.01
Propensity Score	1.00 (0.91–1.13)	0.54
Platinum + 5FU vs. Taxanes + 5FU	1.00 (0.89– 1.13)	0.50
Other Chemo vs. Taxanes + 5FU	1.08 (0.96–1.22)	0.90
Stage 3–4 Cancer	1.259 1.131 1.402	1.00
Diabetes	1.15 (1.03–1.27)	>.99
Location 3	1.07 (0.94– 1.24)	0.86
Smoking Status	1.08 (0.97– 1.18)	0.92
BMI	0.89 (0.79– 1.01)	0.03
Performance Score	0.86 (0.78– 0.96)	<.01
Adeno Histology	1.16 (1.03– 1.33)	0.99
Induction Chemotherapy	0.89 (0.79–0.99)	0.01

* PHE = Posterior probability of a harmful effect. PBE = 1 – PHE – probability of a beneficial effect,

Table 4

Fitted Bayesian regression models for time to Pleural or Pericardial Effusion or death.

Variable	Posterior Quantities for Time to Death or Pleural Effusion		Posterior Quantities for Time to Death or Pericardial Effusion	
	Median HR (95% CI)	PHE	Median HR (95% CI)	PHE
IMRT	0.86 (0.76–0.97)	<.01	0.86 (0.77–0.96)	<.01
Propensity Score	1.00 (0.91–1.12)	0.50	1.00 (0.91–1.12)	0.54
Platinum + 5FU vs. Taxanes + 5FU	1.00 (0.90–1.13)	0.51	1.00 (0.89–1.12)	0.53
Other Chemo vs. Taxanes + 5FU	1.09 (0.97–1.20)	0.92	1.09 (0.97–1.22)	0.92
Stage 3–4 Cancer	1.26 (1.12–1.42)	1.00	1.26 (1.13–1.41)	1.00
Diabetes	1.15 (1.02–1.27)	>.99	1.14 (1.03–1.28)	>.99
Location 3	1.07 (0.95–1.23)	0.86	1.08 (0.96–1.24)	0.90
Smoking Status	1.07 (0.97–1.30)	0.90	1.08 (0.96–1.20)	0.91
BMI	0.90 (0.78–1.00)	0.03	0.89 (0.78–1.00)	0.02
Performance Score	0.86 (0.78–0.95)	<.01	0.86 (0.78–0.95)	<.01
Adeno Histology	1.17 (1.03–1.34)	0.99	1.16 (1.02–1.34)	0.99
Induction Chemotherapy	0.89 (0.79–0.99)	0.02	0.89 (0.79–1.00)	0.02

* PHE = Posterior probability of a harmful effect. PBE = 1 – PHE – probability of a beneficial effect,