Stereotactic Body Radiation Therapy Versus Nonradiotherapeutic Ablative Procedures (Laser/Cryoablation and Electrocautery) for Early-Stage Non–Small Cell Lung Cancer

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ABSTRACT

Background: Despite the fact that stereotactic body radiation therapy (SBRT) is the only recommended first-line therapy for inoperable early-stage non–small cell lung cancer (NSCLC), several thermal ablation procedures (TAPs; defined herein as laser/cryoablation and electrocautery) are available. Studies showing outcomes of these procedures and how they compare with SBRT are scarce. We sought to evaluate the comparative efficacy of SBRT versus TAPs using the National Cancer Database (NCDB). **Methods:** The NCDB was queried for patients with early-stage NSCLC who did not undergo surgical resection. Treatment-specific inclusion criteria were applied to select for patients receiving either TAPs or SBRT. Univariate logistic regression and Cox proportional hazards modeling were performed, and Kaplan-Meier curves were generated. Serial propensity matches were performed using a modified greedy 8→n matching 1:1 algorithm.

Results: A total of 27,734 patients were analyzed; 26,725 underwent SBRT and 1,009 underwent TAPs. Patients who received SBRT were older and more likely to have clinical stage IB (vs IA) disease. Despite this, SBRT was associated with longer median overall survival (mOS; 37.7 vs 33.5 months; $P=.001$) and 1-, 2-, and 5-year OS rates compared with the TAPs cohort (86.7% vs 83.1%, 67.5% vs 62.7%, and 30.6% vs 26.9%, respectively; $P=.001$). Upon propensity matching, improved OS with SBRT remained, with a mOS of 40.4 versus 33.4 months and 1-, 2-, and 5-year OS rates of 89.0% versus 82.9%, 69.7% versus 62.7%, and 34.4% versus 26.4%, respectively ($P=.003$).

Conclusions: Despite being associated with more higher-risk factors, SBRT was associated with higher OS compared with TAPs for treatment of nonoperative patients diagnosed with early-stage NSCLC. However, causation cannot be implied owing to the inherent limitations of large heterogeneous datasets such as the NCDB.

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Background

Patients diagnosed with early-stage non–small cell lung cancer (NSCLC) have multiple evidence-based treatment options. Although lobectomy remains the standard of care in medically operable patients, up to 85% to 90% are not surgical candidates at the time of diagnosis, owing mostly to comorbidities such as chronic obstructive pulmonary disease, heart disease, ongoing tobacco abuse, or patient preference.¹ Classically, these patients were treated with conventionally fractionated radiation therapy (RT), which provided suboptimal local control rates.^{2,3} In recent years, stereotactic body RT (SBRT; also known as stereotactic ablative RT), has gained momentum for this purpose.^{4–6} To date, multiple prospective trials have reported local control rates of at least 90% at 1 year and >80% at 3 years, with largely an absence of significant high-grade toxicities.^{7–10} Furthermore, a pooled analysis from 2 prospective clinical trials reported that SBRT may produce equivalent or even superior outcomes compared with surgical resection for operable patients.¹¹ Although these findings are supportive of SBRT, it should be noted that neither study completed patient accrual, and the analysis was performed in an unplanned manner on the patients who did enroll.¹² Thus, most current evidence for SBRT remains in the setting of inoperability, and its utility in patients who could otherwise undergo resection is under intense investigation (ie, the STABLE-MATES and VALOR trials; ClinicalTrials.gov identifiers: NCT02468024 and NCT02984761, respectively).

SBRT is the current recommended first-line therapy for inoperable early-stage NSCLC, with thermal ablation procedures (TAPs) that do not involve ionizing radiation being available for select patients. TAPs include radiofrequency ablation (RFA), microwave ablation (MWA),

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electrocautery, cryoablation, and electroporation.^{13,14} Due to the novelty and rapid acceptance of SBRT, outcomes data from these procedures are scarce. Early (and largely single-institutional) studies using TAPs reported local control rates of 42% to 69%, along with relatively high rates of treatment-associated toxicities, particularly pneumothorax (42%–63%) and chest tube placement (7%–63%).^{15–17} In a retrospective comparison of RFA versus wedge resection, Ambrogi et al¹⁸ observed suboptimal local control (77% vs 98%), 2-year OS (72% vs 96%), and 3-year OS (35% vs 52%) with RFA.

Two phase II trials attempted to assess the efficacy of TAPs in inoperable patients with early-stage NSCLC. In 2008, the prospective, intention-to-treat, multicenter RAPTURE trial involving 105 patients with 183 tumors treated with RFA reported a 2-year OS of 48% and a 26% rate of postprocedure pneumothorax requiring chest tube placement. Additionally, although no long-term local control data were presented, 88% of patients had a complete response in the treated lesion at 1 year after treatment. Importantly though, only 33 of the included patients were diagnosed with NSCLC, with the remainder being treated for pulmonary metastases, thus limiting the interpretability of the presented efficacy of TAPs.¹⁹ More recently, ACOSOG Z4033 reported a 2-year local control rate of 60% and a 2-year OS of 70% in 54 patients with stage IA NSCLC treated with RFA.¹³ Consistent with past results, 22% of treated patients experienced grade ≥ 3 toxicities.

Recognizing the dearth of comparative data with SBRT, Ochiai et al²⁰ conducted a small retrospective analysis of 95 patients with stage I NSCLC undergoing either RFA (n=48) or SBRT (n=47). Their data indicated similar rates of 3-year local failure (10% vs 7%; $P=.746$) and OS (86% vs 80%; $P=.738$), with nearly identical rates of grade ≥ 3 toxicity in both treatment arms. Conversely, Bi et al²¹ provided a meta-analysis of trials published from 2001 through 2012 using either RFA (n=13) or SBRT (n=31) for the treatment of stage I NSCLC and found that RFA was associated with worse local control at 1 (77% vs 97%), 2 (48% vs 92%), 3 (55% vs 88%), and 5 years (42% vs 86%); however, this did not translate into statistical OS differences. Importantly, SBRT was also noted to have significantly reduced rates of grade ≥ 3 toxicities (2%) compared with RFA (31%).

Multidisciplinary discussion panels and patients often consider TAPs as an alternative to SBRT, with few large-volume assessments to guide clinical decision-making. Our study sought to evaluate the comparative efficacy of SBRT versus TAPs using the National Cancer Database (NCDB).

Methods

The NCDB is a joint project of the Commission on Cancer (CoC) of the American College of Surgeons and the

American Cancer Society that consists of information regarding tumor characteristics, patient demographics, and patient survival for approximately 70% of the US population.^{22–24} The NCDB contains information not included in the SEER database, including details regarding use of systemic therapy. The American College of Surgeons and CoC have not verified and are not responsible for the analytic or statistical methodology used or the conclusions drawn from these data. Because all patient information in the NCDB database is de-identified, this study was exempt from Institutional Review Board evaluation.

The NCDB NSCLC database (2004–2014) was used for this study. Patients with early-stage NSCLC were identified using the following inclusion criteria: (1) clinical stage I disease, (2) pathologically confirmed disease, and (3) no surgical resection. The following exclusion criteria were then applied: clinical stage other than I (ie, I, IA, or IB), pathologic or clinical diagnosis of nodal disease (including coding for regional nodal positivity), missing information regarding vital and outcome status, intervention with palliative intent, and prior administration of chemotherapy. Finally, treatment-specific criteria were applied so that patients received either TAPs, defined as laser ablation/cryotherapy (surgical code 12) or electrocautery (surgical code 13), or SBRT (using regional treatment modality-specific codes), with defined doses for stereotactic treatment of 48, 50, 54, or 60 Gy (see supplemental eTable 1, available with this article at JNCCN.org).

In accordance with the variables in NCDB files, information collected on each patient broadly included demographic, clinical, and treatment data, as well as survival outcomes. All statistical analyses were performed using SAS 9.4 (SAS Institute Inc.). All tests were conducted in a 2-sided manner, with $P<.05$ considered statistically significant. Univariate logistic regression was performed to determine variables associated with receiving SBRT. Any variable with a P value $\leq .10$ was considered in a subsequent logistic regression multivariable model using a backward selection approach, with an $\alpha=.1$ for variable retention in the final model. Similarly, a Cox proportional hazard (Cox PH) model was generated to identify variables associated with survival among the entire cohort of patients, and all variables of interest were then included in a multivariable Cox PH model. Patients denoted as alive were treated as censored in all survival analyses. Kaplan-Meier curves were constructed to illustrate differences in survival between treatment cohorts, and OS and median OS (mOS) were assessed using log-rank testing.

Propensity matching was used to account for any bias that may have led patients to receive one treatment modality over the other (TAPs vs SBRT). Using variables

outlined in the logistic regression procedure described earlier and any other clinically relevant variable, a modified greedy 8→n (ie, greedy 8→7... greedy 8→1) matching 1:1 algorithm was implemented. For propensity matching, Charlson-Deyo comorbidity scores were counted individually instead of combined into groups to ensure optimal matching. Various propensity-matched models were constructed to balance matching completeness with goodness of fit. In efforts to perform the highest quality of propensity matching, unmatched patients and any matches that demonstrated a >2% difference in propensity scores were eliminated from further analysis. Patient demographics were reassessed for each model chosen using appropriate paired tests (ie, paired *t* testing, McNemar testing, etc.) and compared with the original patient population. Additionally, Kaplan-Meier curves were used to describe any difference in OS between treatment cohorts.

Results

A total of 27,734 patients met study criteria, including 26,725 patients (96%) who underwent SBRT and 1,009 (4%) who underwent TAPs (Figure 1). Patients had a relatively even distribution in terms of sex, but were predominately white. On multivariable analysis, characteristics that remained associated with receipt of SBRT were geographic region of the treating facility, receiving treatment at an academic institute versus a community cancer center, older age, a more recent diagnosis, having clinical stage IB disease, and histologic subtype (Table 1 and supplemental eTable 2).

Median follow-up was 26.7 months, with 43.9% of patients recorded as alive. Rates of 30- and 90-day mortality for SBRT versus TAPs were 0.01% versus 0.7% and 0.5% versus 3.8%, respectively. On Cox PH analysis, receipt of SBRT, younger age, female sex, black race, lower Charlson-Deyo comorbidity scores, histology other than squamous, lower tumor grade, and clinical stage IA versus IB disease were associated with reduced hazards for death (Table 2 and supplemental eTable 3). On Kaplan-Meier analysis, OS rates were significantly longer in patients treated with SBRT compared with those treated with TAPs (1-year OS: 86.7% [95% CI, 86.3%–87.1%] vs 83.1% [80.6%–85.3%]; 2-year OS: 67.5% [66.9%–68.1%] vs 62.7% [59.6%–65.7%]; and 5-year OS: 30.6% [29.9%–31.4%] vs 26.9% [23.7%–30.2%]; *P* = .001; Figure 2 and supplemental eFigure 1). This corresponded to an mOS of 37.7 months (95% CI, 37.2–38.3) and 33.5 months (95% CI, 30.9–36.5) for each group, respectively (*P* = .001).

To minimize bias within the data, 1:1 propensity matching using a greedy 8→1 algorithm was performed. After excluding any matches with >2% difference in propensity scores, 987 pairs (97.8% of all patients treated

Figure 1. Patient selection flowchart.

Abbreviations: NSCLC, non-small cell lung cancer; SBRT, stereotactic body radiation therapy; TAPs, thermal ablative procedures.

with TAPs) were included for subsequent analysis. Models based solely on 8-digit nearest-neighbor matches and sequential greedy matching 8→7 to 8→1 were also generated. Matching completeness and goodness of matches were analyzed for each of these models (supplemental eTable 4). Greedy 8→6 matching resulted in only 22% of patient inclusion, whereas greedy 8→5 incorporated >60% of possible matched pairs. Greedy 8→4 further increased the patient inclusion to nearly 85%, but had a near logarithmic increase in average difference in propensity scores. Despite the difference in propensity scores, greedy 8→5, greedy 8→4, and greedy 8→1 displayed median ages of 75.0 years for patients who underwent SBRT or TAPs, with demographics varying only slightly between models. The greedy 8→4 model was selected as the comparison model that balanced patient inclusion with best matching pairs (Table 3 and supplemental eTable 5). After greedy 8→4 matching, univariable logistic regression revealed similar clinical characteristics between cohorts, although tumor size

Table 1. Patient Demographics

Parameter	SBRT (N=26,725)	TAPs (N=1,009)	Univariable ^a		Multivariable ^a	
			OR (95% CI)	P Value	OR (95% CI)	P Value
Median age (IQR), y	75.0 (69–81)	74.0 (67–81)	1.015 (1.008–1.022)	<.001	1.012 (1.005–1.020)	.001
Sex						
Male	12,460 (46.6)	485 (48.1)	Ref		Ref	
Female	14,265 (53.4)	524 (51.9)	1.060 (0.934–1.202)	.367	0.891 (0.782–1.014)	.080
Facility type						
Academic institute	11,751 (44.0)	496 (49.2)	Ref		Ref	
Community cancer program	822 (3.1)	56 (5.6)	0.619 (0.466–0.824)	<.001	0.506 (0.376–0.682)	.015
Comprehensive community cancer program	10,647 (39.8)	327 (32.4)	1.374 (1.192–1.584)	<.001	1.115 (0.959–1.297)	.643
Integrated network cancer program	3,501 (13.1)	121 (12.0)	1.221 (0.998–1.495)	.862	1.113 (0.895–1.383)	.783
Unknown	4 (0.0)	9 (0.9)				
Facility location						
New England	1,447 (5.4)	159 (15.8)	Ref		Ref	
Middle Atlantic	4,110 (15.4)	211 (20.9)	2.141 (1.728–2.653)	<.001	2.160 (1.732–2.695)	<.001
South Atlantic	5,934 (22.2)	193 (19.1)	3.379 (2.718–4.200)	<.001	3.452 (2.746–4.339)	<.001
East North Central	5,351 (20.0)	177 (17.5)	3.322 (2.661–4.147)	<.001	3.394 (2.690–4.283)	<.001
East South Central	1,670 (6.2)	63 (6.2)	2.913 (2.158–3.933)	<.001	2.543 (1.865–3.468)	<.001
West North Central	3,355 (12.6)	45 (4.5)	8.193 (5.851–11.472)	<.001	9.193 (6.523–12.954)	<.001
West South Central	1,512 (5.7)	72 (7.1)	2.308 (1.731–3.077)	<.001	2.566 (1.905–3.457)	<.001
Mountain	996 (3.7)	27 (2.7)	4.054 (2.674–6.144)	<.001	3.714 (2.427–5.683)	<.001
Pacific	2,346 (8.8)	53 (5.3)	4.866 (3.542–6.686)	<.001	4.525 (3.257–6.289)	<.001
Unknown	4 (0.0)	9 (0.9)				
Histology						
Squamous	9,160 (34.3)	334 (33.1)	Ref		Ref	
Adenocarcinoma	11,672 (43.7)	418 (41.4)	1.018 (0.880–1.179)	.584	1.059 (0.909–1.235)	.047
Non–small cell NOS	4,457 (16.7)	145 (14.4)	1.121 (0.919–1.366)	.255	1.446 (1.173–1.783)	<.001
Other	1,436 (5.4)	112 (11.1)				
Median year of diagnosis (IQR)	2012 (2010–2013)	2010 (2008–2012)	1.289 (1.258–1.321)	<.001	1.334 (1.299–1.369)	<.001
Clinical stage						
IA	19,856 (74.3)	821 (81.4)	Ref		Ref	
IB	5,659 (21.2)	135 (13.4)	1.733 (1.441–2.084)	<.001	1.860 (1.538–2.249)	<.001
“I” NOS	1,210 (4.5)	53 (5.2)	0.944 (0.711–1.254)	.231	0.967 (0.719–1.299)	.251
Tumor grade						
1	2,156 (8.1)	91 (9.0)	Ref		Ref	
2	4,446 (16.6)	183 (18.1)	1.025 (0.793–1.325)	.603	0.872 (0.663–1.145)	.055
3	5,052 (18.9)	171 (16.9)	1.247 (0.962–1.616)	.771	1.164 (0.883–1.536)	.515
4	95 (0.4)	6 (0.7)	0.668 (0.285–1.566)	.253	1.311 (0.536–3.210)	.603
Unknown	14,976 (56.0)	558 (55.3)				

Statistically significant *P* values are bold.

Abbreviations: IQR, interquartile range; NOS, not otherwise specified; OR, odds ratio; SBRT, stereotactic body radiation therapy; TAPs, thermal ablative procedures.

^aEnd point: receipt of SBRT.

could still not be adequately matched and remained statistically lower in the TAP group.

Cox PH analysis of the 8→4 matched data showed that the following were associated with a lower hazard for

death: receipt of SBRT compared with TAPs, younger age, female sex, lower Charlson-Deyo comorbidity score, facility location, histology other than squamous cell, lower tumor grade, smaller tumor size, and less advanced

Table 2. Cox Proportional Analysis of Hazards for Death

Parameter	Univariable			Multivariable		
	HR	95% CI	P Value	HR	95% CI	P Value
Treatment (TAPs vs SBRT)	1.136	1.052–1.226	.001	1.330	1.171–1.510	<.001
Age (continuous)	1.015	1.013–1.017	<.001	1.013	1.010–1.017	<.001
Sex (female vs male)	0.750	0.727–0.774	<.001	0.778	0.739–0.818	<.001
Race						
Black vs white	0.848	0.798–0.900	<.001	0.868	0.786–0.959	.006
Indian vs white	1.164	0.866–1.565	.314	1.146	0.728–1.802	.556
Pacific Islander vs white	0.669	0.470–0.999	.019	0.836	0.617–1.131	.245
Charlson-Deyo comorbidity score (≥ 3 vs 0–2)	1.594	1.487–1.708	<.001	1.539	1.383–1.712	<.001
Facility location						
Middle Atlantic vs New England	0.928	0.860–1.005	.056	0.949	0.826–1.091	.464
South Atlantic vs New England	0.964	0.897–1.037	.329	0.965	0.845–1.103	.606
East North Central vs New England	1.033	0.960–1.112	.383	1.019	0.892–1.163	.783
East South Central vs New England	1.090	0.996–1.193	.062	0.998	0.851–1.170	.977
West North Central vs New England	1.016	0.939–1.098	.693	1.005	0.879–1.150	.939
West South Central vs New England	0.863	0.786–0.947	.002	0.883	0.757–1.030	.114
Mountain vs New England	0.971	0.875–1.078	.584	0.944	0.795–1.120	.507
Pacific vs New England	0.902	0.828–0.983	.018	0.871	0.750–1.012	.071
Histology						
Adenocarcinoma vs squamous	0.726	0.700–0.753	<.001	0.828	0.782–0.877	<.001
Non-small vs squamous	0.859	0.821–0.899	<.001	0.903	0.823–0.991	.031
Tumor grade						
2 vs 1	1.415	1.317–1.520	<.001	1.291	1.188–1.403	<.001
3 vs 1	1.475	1.375–1.582	<.001	1.309	1.203–1.425	<.001
4 vs 1	1.308	1.010–1.693	.042	1.151	0.782–1.694	.477
Tumor size (continuous)	1.003	1.003–1.003	<.001			
Clinical stage (IB vs IA)	1.462	1.410–1.517	<.001	1.440	1.361–1.524	<.001

Statistically significant *P* values are bold.

Abbreviations: HR, hazard ratio; SBRT, stereotactic body radiation therapy; TAPs, thermal ablative procedures.

clinical stage (IA vs IB; supplemental eTable 6). On multivariable analysis, only receipt of SBRT versus TAPs, younger age, lower Charlson-Deyo comorbidity score, and less advanced clinical stage remained significantly associated with a decreased hazard ratio (supplemental eTable 6). Of note, tumor size was excluded from the multivariable analysis due to its correlation with clinical stage. Subsequent survival analyses revealed mOS of 40.4 versus 33.4 months, and 1-, 2-, and 5-year OS of 89.0% versus 82.9%, 69.7% versus 62.7%, and 34.4% versus 26.4% between the SBRT and TAPs cohorts, respectively ($P=.0033$; Figure 3 and stratification for T stage in supplemental eFigure 2). Both the greedy 8→1 and 8→5 models demonstrated similar results (supplemental eFigure 3 and eTable 7).

To determine whether the reduced OS associated with TAPs was due to higher rates of acute iatrogenic

toxicity associated with these procedures compared with SBRT, Kaplan-Meier analyses were performed, excluding all patients who died within 6 months of their respective procedures. Unmatched and propensity-matched data generated using greedy 8→1, 8→4, and 8→5 models showed that patients who underwent SBRT had a persistent OS advantage compared with their TAPs counterparts (data not shown).

Discussion

Because a significant proportion of patients with early-stage NSCLC are not candidates for surgical resection, noninvasive methods such as SBRT or TAPs are important alternative treatment options. Primarily due to treatment novelty, no large-scale clinical trials have attempted to compare currently available noninvasive treatments for NSCLC in terms of patient outcomes.

Figure 2. Kaplan-Meier curve of overall survival for patients undergoing SBRT versus TAPs-based procedures.

Abbreviations: SBRT, stereotactic body radiation therapy; TAPs, thermal ablative procedures.

Consequently, patient and provider decision-making between available treatment options has been limited to comparative analyses across various single-modality prospective studies or small-scale retrospective analyses. Our study addresses this knowledge gap and demonstrates that SBRT may be associated (without implying causation) with improved OS compared with TAPs.

Through the use of data collected in the NCDB, we were able to analyze outcomes for 27,734 patients with early-stage NSCLC treated with either SBRT or TAPs. In this cohort, patients who received TAPs tended to be younger and have lower-stage disease with similar Charlson-Deyo comorbidity scores, indicating a potential difference in patient populations being treated with TAPs compared with SBRT. As such, treatment with SBRT was associated with a slightly longer mOS of 4.2 months. On propensity matching, cohorts were nearly identical, and the survival difference between treatment groups was even more pronounced (7.0 months). These findings suggest an inherent selection bias against SBRT (ie, favoring TAPs), despite which SBRT remained associated with higher mOS.

There are several potential reasons for the improved OS with SBRT. Increased local failure may increase the risk of cancer-specific death through local progression or development of associated distant metastatic disease. Another potential explanation is that SBRT has been associated with incidental mediastinal dose, which may have meaningful implications with regard to treatment of occult regional metastatic disease, a concept which would not be present in the setting of TAPs.²⁵

One big confounder that must also be considered is the difference in patient populations. For example, was the reason for not being surgical candidates similar between cohorts? Additionally, TAPs may be considered

as alternatives for patients who may not be eligible for SBRT, and these patients may have more comorbidities and a higher risk of mortality, leading to a negative skewing of survival data. Although this is a seemingly plausible scenario, very few inoperable patients who cannot undergo SBRT would actually be candidates for TAPs. After matching for as many variables present in NCDB, including Charlson-Deyo comorbidity scores, differences in survival between TAPs and SBRT were even more pronounced. Furthermore, the intent of each therapy may be different. For example, providers offering SBRT may be doing so with a curative intent, whereas providers of TAPs may be offering the procedure for palliation. If this was true, one would suspect that the cancer was disseminated, that the tumor was larger, or some other reason why TAPs may be more appropriate than SBRT. Although we were unable to establish a reason why each modality was offered to each patient, cancer and tumor characteristics (ie, stage, size) were similar between cohorts. Thus, there may be a reason why the TAPs cohort received TAPs over SBRT; however, due to limited data provided in the NCDB, we cannot ascertain why, only that patients between cohorts are similar by all metrics included in the NCDB.

Other studies have compared TAPs with SBRT,²⁶ but had major shortcomings that severely hampered the conclusions, including lack of describing prematching survival, matching, and goodness-of-fit methodologies, and a lack of multivariate analysis. To this extent, the multiple propensity-matching algorithms we used should be considered a more robust way to control unforeseen biases. However, despite the flawed methodologies in other such studies, we posit that TAPs can be excellent alternatives to SBRT in the re-irradiation setting for post-SBRT isolated local recurrences.²⁷

Overall, limitations in this work are varied. Foremost, despite use of multivariate analyses and propensity matching, the retrospective design of this study never entirely eliminates the presence of potential bias that cannot be accounted for. As such, we cannot ensure that patient populations between the cohorts are truly identical, which is a limitation of the NCDB. Additionally, because NCDB data depend on precise diagnosis and treatment coding, possible mistakes made during data input may result in patients being erroneously included within the analyzed groups. Due to the coding provided, the NCDB also prevents thorough analysis into the individual TAPs and thus does not allow each technique to be directly compared with SBRT. Moreover, due to its retrospective and large-scale design, the NCDB disallows assessment of whether SBRT or TAPs were provided to the analyzed patients in a technically sound manner. Furthermore, the NCDB only allows for analysis of OS,

Table 3. Patient Demographics for Propensity-Matched Patients Using the Greedy 8→4 Model

Parameter	SBRT (N=853) n (%)	TAPs (N=853) n (%)	Univariable ^a
			P Value
Median age (IQR), y	75.0 (69–80)	74.0 (68–81)	
Sex			
Male	405 (47.5)	411 (48.2)	
Female	448 (52.5)	442 (51.8)	
Facility type			
Academic institute	410 (48.1)	398 (46.7)	
Community cancer program	45 (5.3)	43 (5.0)	
Comprehensive community cancer program	287 (33.6)	299 (35.1)	
Integrated network cancer program	111 (13.0)	113 (13.2)	
Unknown	—	—	
Facility location			
New England	89 (10.4)	80 (9.4)	
Middle Atlantic	174 (20.4)	180 (21.1)	
South Atlantic	161 (18.9)	179 (21.0)	
East North Central	183 (21.5)	172 (20.2)	
East South Central	45 (5.3)	56 (6.6)	
West North Central	52 (6.1)	43 (5.0)	
West South Central	69 (8.1)	66 (7.7)	
Mountain	33 (3.9)	27 (3.2)	
Pacific	47 (5.5)	50 (5.9)	
Unknown	—	—	
Histology			
Squamous	264 (30.9)	293 (34.3)	
Adenocarcinoma	405 (47.5)	362 (42.5)	
Non–small cell NOS	113 (13.2)	122 (14.3)	
Other	71 (8.4)	76 (8.9)	
Mean year of diagnosis (IQR)	2012 (2010–2013)	2010 (2008–2012)	
Median tumor size (IQR), mm	21 (15–29)	18 (14–25)	<.001
Clinical stage			
IA	680 (79.7)	682 (80.0)	
IB	122 (14.3)	126 (14.8)	
“I” NOS	51 (6.0)	45 (5.3)	
Tumor grade			
1	81 (9.5)	74 (8.7)	
2	148 (17.4)	162 (19.0)	
3	171 (20.0)	159 (18.6)	
4	2 (0.2)	5 (0.6)	
Unknown	451 (52.9)	453 (53.1)	

Statistically significant *P* values are bold.

Abbreviations: IQR, interquartile range; NOS, not otherwise specified; OR, odds ratio; SBRT, stereotactic body radiation therapy; TAPs, thermal ablative procedures.

^aEnd point: receipt of SBRT.

without any indication of local or regional progression-free survival, development of distant metastatic disease, toxicities, or cause of death. Additionally, the potential to

have missed patients based on NCDB coding for dose should be mentioned, because SBRT dosing is largely delivered to a particular volume or isodose line, which

Figure 3. Kaplan-Meier curve of overall survival for propensity-matched patients using greedy 8→4 matching.
Abbreviations: SBRT, stereotactic body radiation therapy; TAPs, thermal ablative procedures.

could alter the delivered dose to another isodose line or volume and thus would have been incompletely captured by this study. Lastly, we compared all available patients treated with TAPs as coded in the NCDB. However, cryoablation and laser ablation are coded using the same identifier, MWA and RFA are not uniquely coded in the lung NCDB, and there is a category termed “local tumor destruction, not otherwise specified” (supplemental eFigure 4). Therefore, it is impossible to determine outcomes for each of the TAPs individually, which may vary greatly. This is another large limitation of NCDB.

Despite these limitations, this study is an important step in understanding the nonsurgical management of

early-stage NSCLC and provides impetus for multiple further studies. Most importantly, these results should be validated in a prospective manner. Further investigation is required to elucidate the cause of shorter OS with TAPs, in order to better delineate whether it is due to iatrogenic mortality, cancer-related death, or other causes. Additionally, patient outcomes should be separately compared across the various TAPs, including RFA, MWA, and electroporation, to determine whether one technique provides relatively better disease control or survival and thus may alone be equivalent to SBRT.

Conclusions

Results of our analysis suggest that, compared with TAPs, SBRT may be associated with longer OS in the treatment of nonoperative patients diagnosed with early-stage NSCLC. However, causation cannot be implied owing to the inherent limitations of large heterogeneous datasets such as the NCDB.

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Supplemental online content for:

Stereotactic Body Radiation Therapy Versus Nonradiotherapeutic Ablative Procedures (Laser/Cryoablation and Electrocautery) for Early-Stage Non–Small Cell Lung Cancer

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eFigure 1: Kaplan-Meier Curve of Different Stereotactic Body Radiation Doses Comprising SBRT Cohort, and Different Thermal Ablation Procedures Comprising the TAPs Cohort

eFigure 2: Kaplan-Meier Curve for T1 and T2 Disease Between SBRT and TAPs Cohorts

eFigure 3: Kaplan-Meier Curve of Overall Survival for Propensity-Matched Patients Using Greedy 8→1 and 8→5 Matching

eFigure 4: Kaplan-Meier Curve of Different Thermal Ablation Procedures Available in the NCDB

eTable 1: Dose and Fractionation Patterns of the SBRT Cohort

eTable 2: Complete List of Patient Demographics

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eTable 7: OS of SBRT vs TAPs Cohorts Across Matching Models

eFigure 1. Kaplan-Meier curve of different stereotactic body radiation doses comprising the SBRT cohort, and different thermal ablation procedures comprising the TAPs cohort (ie, elec and laser).

Abbreviations: Elec, electrocautery; SBRT, stereotactic body radiotherapy; TAPs, thermal ablative procedures.

eFigure 2. Kaplan-Meier curve for (A) T1 and (B) T2 disease between SBRT and TAPs cohorts.

Abbreviations: SBRT, stereotactic body radiation therapy; TAPs, thermal ablative procedures.

eFigure 3. Kaplan-Meier curve of overall survival for propensity-matched patients using (A) greedy 8→1 and (B) 8→5 matching. Abbreviations: SBRT, stereotactic body radiation therapy; TAPs, thermal ablative procedures.

eFigure 4. Kaplan-Meier curve of different thermal ablation procedures available in the NCDB, including (A) “local tumor destruction, not otherwise specified” and (B) compiling these into a new, theoretical TAPs cohort. Abbreviations: ab, ablation; cryoab, cryoablation; NCDB, National Cancer Database; SBRT, stereotactic body radiation therapy; TAPs, thermal ablative procedures.

eTable 1. Dose and Fractionation Patterns of the SBRT Cohort (N=26,725)

	N (%)
Dose, Gy	
48	5,727 (21.4%)
50	9,677 (36.2%)
54	4,368 (16.3%)
60	6,953 (26.0%)
Fractions	
3	7,835 (29.3%)
4	7,212 (27.0%)
5	9,291 (34.8%)
Other	2,387 (8.9%)

Abbreviation: SBRT, stereotactic body radiation therapy.

eTable 2. Complete List of Patient Demographics

Parameter	SBRT (N=26,725)	TAPs (N=1,009)	Univariable*		Multivariable*	
			OR (95% CI)	P Value	OR (95% CI)	P Value
Median age (IQR), y	75.0 (69–81)	74.0 (67–81)	1.015 (1.008–1.022)	<.001	1.012 (1.005–1.020)	.001
Sex						
Male	12,460 (46.6)	485 (48.1)	Ref		Ref	
Female	14,265 (53.4)	524 (51.9)	1.060 (0.934–1.202)	.367	0.891 (0.782–1.014)	.080
Race						
White	23,861 (89.3)	926 (91.8)	Ref			
Black	2,230 (8.3)	64 (6.3)	1.353 (1.046–1.749)	.948		
Indian	76 (0.3)	0 (0.0)				
Pacific Islander	258 (1.0)	10 (1.0)	1.001 (0.531–1.889)	.972		
Other	72 (0.3)	0 (0.0)				
Missing	228 (0.9)	9 (0.9)				
Charlson-Deyo comorbidity score						
0–2	25,485 (95.4)	960 (95.1)	Ref			
≥3	1,240 (4.6)	49 (4.9)	0.953 (0.711–1.277)	.748		
Insurance type						
Not insured	194 (0.7)	9 (0.9)	0.903 (0.454–1.799)	.272		
Private insurance	3,436 (12.9)	144 (14.3)	Ref			
Medicaid	803 (3.0)	35 (3.5)	0.963 (0.660–1.404)	.128		
Medicare	21,017 (78.6)	797 (79.0)	1.105 (0.922–1.325)	.225		
Other government	942 (3.5)	14 (1.4)	2.817 (1.620–4.899)	<.001		
Unknown	333 (1.2)	10 (1.0)	1.396 (0.728–2.675)	.689		
Income						
<\$38,000	4,765 (17.8)	177 (17.5)	Ref			
\$38,000–\$47,999	6,746 (25.2)	253 (25.1)	0.990 (0.814–1.204)	.863		
\$48,000–\$62,999	7,434 (27.8)	230 (22.8)	1.201 (0.984–1.465)	.999		
≥\$63,000	7,608 (28.5)	336 (33.3)	0.841 (0.699–1.013)	.999		
Unknown	172 (0.6)	13 (1.3)				
Location, population						
≥1 million	13,116 (49.1)	466 (46.2)	Ref			
250,000–1 million	5,980 (22.4)	209 (20.7)	1.016 (0.861–1.200)	.514		
Metro with <250,000	2,487 (9.3)	98 (9.7)	0.902 (0.722–1.126)	.124		
Urban >20,000, adjacent to metro	1,301 (4.9)	61 (6.0)	0.758 (0.577–0.995)	.010		
Urban >20,000, not adjacent to metro	369 (1.4)	9 (0.9)	1.456 (0.747–2.840)	.339		
Urban 2,500–20,000, adjacent to metro	1,524 (5.7)	60 (5.9)	0.902 (0.686–1.187)	.189		
Urban 2,500–20,000, not adjacent to metro	724 (2.7)	24 (2.4)	1.072 (0.706–1.626)	.949		
Rural <2,500, adjacent to metro	254 (1.0)	6 (0.6)	1.504 (0.666–3.397)	.382		
Rural <2,500, not adjacent to metro	320 (1.2)	8 (0.8)	1.421 (0.700–2.883)	.408		
Unknown	650 (2.4)	68 (6.7)				

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Statistically significant *P* values are bold.

Abbreviations: IQR, interquartile range; metro, metropolitan area; NA, not available; NOS, not otherwise specified; OR, odds ratio; SBRT, stereotactic body radiation therapy; TAPs, thermal ablative procedures.

*End point: receipt of SBRT.

eTable 2. Complete List of Patient Demographics (cont.)

Parameter	SBRT (N=26,725)	TAPs (N=1,009)	Univariable ^a		Multivariable ^a	
			OR (95% CI)	P Value	OR (95% CI)	P Value
Residents in ZIP code without high school diploma						
≥29%	3,866 (14.5)	129 (12.8)	Ref			
20%–28.9%	7,147 (26.7)	257 (25.5)	0.928 (0.748–1.151)	.681		
14%–19.9%	9,438 (35.3)	377 (37.4)	0.836 (0.682–1.024)	.108		
<14%	6,110 (22.9)	234 (23.2)	0.871 (0.700–1.084)	.497		
Unknown	164 (0.6)	12 (1.2)				
Facility type						
Academic institute	11,751 (44.0)	496 (49.2)	Ref		Ref	
Community cancer program	822 (3.1)	56 (5.6)	0.619 (0.466–0.824)	<.001	0.506 (0.376–0.682)	.015
Comprehensive community cancer program	10,647 (39.8)	327 (32.4)	1.374 (1.192–1.584)	<.001	1.115 (0.959–1.297)	.643
Integrated network cancer program	3,501 (13.1)	121 (12.0)	1.221 (0.998–1.495)	.862	1.113 (0.895–1.383)	.783
Unknown	4 (0.0)	9 (0.9)				
Facility location						
New England	1,447 (5.4)	159 (15.8)	Ref		Ref	
Middle Atlantic	4,110 (15.4)	211 (20.9)	2.141 (1.728–2.653)	<.001	2.160 (1.732–2.695)	<.001
South Atlantic	5,934 (22.2)	193 (19.1)	3.379 (2.718–4.200)	<.001	3.452 (2.746–4.339)	<.001
East North Central	5,351 (20.0)	177 (17.5)	3.322 (2.661–4.147)	<.001	3.394 (2.690–4.283)	<.001
East South Central	1,670 (6.2)	63 (6.2)	2.913 (2.158–3.933)	<.001	2.543 (1.865–3.468)	<.001
West North Central	3,355 (12.6)	45 (4.5)	8.193 (5.851–11.472)	<.001	9.193 (6.523–12.954)	<.001
West South Central	1,512 (5.7)	72 (7.1)	2.308 (1.731–3.077)	<.001	2.566 (1.905–3.457)	<.001
Mountain	996 (3.7)	27 (2.7)	4.054 (2.674–6.144)	<.001	3.714 (2.427–5.683)	<.001
Pacific	2,346 (8.8)	53 (5.3)	4.866 (3.542–6.686)	<.001	4.525 (3.257–6.289)	<.001
Unknown	4 (0.0)	9 (0.9)				
Median distance to treating facility (IQR), mi	11.3 (4.9–28.9)	10.8 (4.7–26.6)	(Continuous)	.143		
Histology						
Squamous	9,160 (34.3)	334 (33.1)	Ref		Ref	
Adenocarcinoma	11,672 (43.7)	418 (41.4)	1.018 (0.880–1.179)	.584	1.059 (0.909–1.235)	.047
Non–small cell NOS	4,457 (16.7)	145 (14.4)	1.121 (0.919–1.366)	.255	1.446 (1.173–1.783)	<.001
Other	1,436 (5.4)	112 (11.1)				
Median year of diagnosis (IQR)	2012 (2010–2013)	2010 (2008–2012)	1.289 (1.258–1.321)	<.001	1.334 (1.299–1.369)	<.001
Median tumor size (IQR), mm	21 (15–29)	18 (14-25)	1.035 (1.027–1.043)	<.001		
Clinical stage						
IA	19,856 (74.3)	821 (81.4)	Ref		Ref	
IB	5,659 (21.2)	135 (13.4)	1.733 (1.441–2.084)	<.001	1.860 (1.538–2.249)	<.001
“I” NOS	1,210 (4.5)	53 (5.2)	0.944 (0.711–1.254)	.231	0.967 (0.719–1.299)	.251
Tumor grade						
1	2,156 (8.1)	91 (9.0)	Ref		Ref	
2	4,446 (16.6)	183 (18.1)	1.025 (0.793–1.325)	.603	0.872 (0.663–1.145)	.055
3	5,052 (18.9)	171 (16.9)	1.247 (0.962–1.616)	.771	1.164 (0.883–1.536)	.515
4	95 (0.4)	6 (0.7)	0.668 (0.285–1.566)	.253	1.311 (0.536–3.210)	.603
Unknown	14,976 (56.0)	558 (55.3)				

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Statistically significant P values are bold.

Abbreviations: IQR, interquartile range; metro, metropolitan area; NA, not available; NOS, not otherwise specified; OR, odds ratio; SBRT, stereotactic body radiation therapy; TAPs, thermal ablative procedures.

^aEnd point: receipt of SBRT.

eTable 2. Complete List of Patient Demographics (cont.)						
Parameter	SBRT (N=26,725)	TAPs (N=1,009)	Univariable ^a		Multivariable ^a	
			OR (95% CI)	P Value	OR (95% CI)	P Value
Primary site						
Upper lobe	16,091 (60.2)	564 (55.9)	Ref			
Bronchus	94 (0.4)	41 (4.1)	0.080 (0.055–0.117)	<.001		
Middle lobe	1,232 (4.6)	40 (4.0)	1.080 (0.779–1.495)	.962		
Lower lobe	8,691 (32.5)	339 (33.6)	0.899 (0.784–1.031)	.956		
Lung/Bronchus overlap	57 (0.2)	0 (0.0)				
Unknown	560 (2.1)	25 (2.5)				
Tumor laterality						
Right	14,872 (55.6)	529 (52.4)	Ref			
Left	11,739 (43.9)	438 (43.4)	0.953 (0.838–1.085)	.944		
Unknown/NA	114 (0.4)	42 (4.2)				
Mortality						
30-d	3 (0.01%)	7 (0.7%)				
90-d	134 (0.5%)	38 (3.8%)				
6-mo	971 (3.6%)	76 (7.5%)				
Median days after diagnosis until treatment (IQR)	56 (37–84)	44 (22–76)				

Statistically significant *P* values are bold.
Abbreviations: IQR, interquartile range; metro, metropolitan area; NA, not available; NOS, not otherwise specified; OR, odds ratio; SBRT, stereotactic body radiation therapy; TAPs, thermal ablative procedures.
^aEnd point: receipt of SBRT.

eTable 3. Complete Cox Proportional Analysis of Hazards for Death

Parameter	Univariable			Multivariable		
	HR	95% CI	P Value	HR	95% CI	P Value
Treatment (TAPs vs SBRT)	1.136	1.052–1.226	.001	1.330	1.171–1.510	<.001
Age (continuous)	1.015	1.013–1.017	<.001	1.013	1.010–1.017	<.001
Sex (female vs male)	0.750	0.727–0.774	<.001	0.778	0.739–0.818	<.001
Race						
Black vs white	0.848	0.798–0.900	<.001	0.868	0.786–0.959	.006
Indian vs white	1.164	0.866–1.565	.314	1.146	0.728–1.802	.556
Pacific Islander vs white	0.669	0.470–0.999	.019	0.836	0.617–1.131	.245
Charlson-Deyo comorbidity score (≥ 3 vs 0–2)	1.594	1.487–1.708	<.001	1.539	1.383–1.712	<.001
Insurance type						
Not insured vs private insurance	0.890	0.726–1.091	.262			
Medicaid vs private insurance	0.995	0.892–1.110	.925			
Medicare vs private insurance	1.185	1.129–1.244	<.001			
Other government vs private insurance	1.166	1.056–1.287	.002			
Unknown vs private insurance	1.122	0.930–1.306	.140			
Income						
\$38,000–\$47,999 vs $< \$38,000$	1.026	0.977–1.077	.298			
\$48,000–\$62,999 vs $< \$38,000$	1.007	0.960–1.057	.762			
$\geq \$63,000$ vs $< \$38,000$	0.961	0.917–1.008	.105			
Location, population						
250,000–1 million vs ≥ 1 million	1.103	1.059–1.144	<.001			
Metro with $< 250,000$ vs ≥ 1 million	1.135	1.073–1.200	<.001			
Urban $> 20,000$, adjacent to metro vs ≥ 1 million	1.101	1.023–1.185	.010			
Urban $> 20,000$, not adjacent to metro vs ≥ 1 million	1.059	0.921–1.217	.423			
Urban 2,500–20,000, adjacent to metro vs ≥ 1 million	1.106	1.032–1.187	.005			
Urban 2,500–20,000, not adjacent to metro vs ≥ 1 million	1.202	1.092–1.322	<.001			
Rural $< 2,500$, adjacent to metro vs ≥ 1 million	1.183	1.003–1.395	.046			
Rural $< 2,500$, not adjacent to metro vs ≥ 1 million	1.112	0.963–1.285	.148			
Residents in ZIP code without high school diploma						
20%–28.9% vs $\geq 29\%$	0.985	0.935–1.037	.561			
14%–19.9% vs $\geq 29\%$	0.998	0.950–1.048	.925			
$< 14\%$ vs $\geq 29\%$	0.972	0.922–1.025	.290			
Facility type						
Community cancer program vs academic institute	1.074	0.976–1.183	.143			
Comprehensive community cancer program vs academic institute	1.122	1.084–1.162	<.001			
Integrated network cancer program vs academic institute	1.064	1.014–1.117	.012			

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Statistically significant P values are bold.

Abbreviations: HR; hazard ratio; metro, metropolitan area; SBRT, stereotactic body radiation therapy; TAPs, thermal ablative procedures.

eTable 3. Complete Cox Proportional Analysis of Hazards for Death (cont.)

Parameter	Univariable			Multivariable		
	HR	95% CI	P Value	HR	95% CI	P Value
Facility location						
Middle Atlantic vs New England	0.928	0.860–1.005	.056	0.949	0.826–1.091	.464
South Atlantic vs New England	0.964	0.897–1.037	.329	0.965	0.845–1.103	.606
East North Central vs New England	1.033	0.960–1.112	.383	1.019	0.892–1.163	.783
East South Central vs New England	1.090	0.996–1.193	.062	0.998	0.851–1.170	.977
West North Central vs New England	1.016	0.939–1.098	.693	1.005	0.879–1.150	.939
West South Central vs New England	0.863	0.786–0.947	.002	0.883	0.757–1.030	.114
Mountain vs New England	0.971	0.875–1.078	.584	0.944	0.795–1.120	.507
Pacific vs New England	0.902	0.828–0.983	.018	0.871	0.750–1.012	.071
Distance to treating facility (continuous)	1.000	1.000–1.000	.228			
Median year of diagnosis	0.994	0.986–1.001	.090			
Histology						
Adenocarcinoma vs squamous	0.726	0.700–0.753	<.001	0.828	0.782–0.877	<.001
Non–small cell vs squamous	0.859	0.821–0.899	<.001	0.903	0.823–0.991	.031
Tumor grade						
2 vs 1	1.415	1.317–1.520	<.001	1.291	1.188–1.403	<.001
3 vs 1	1.475	1.375–1.582	<.001	1.309	1.203–1.425	<.001
4 vs 1	1.308	1.010–1.693	.042	1.151	0.782–1.694	.477
Tumor size (continuous)	1.003	1.003–1.003	<.001			
Clinical stage (IB vs IA)	1.462	1.410–1.517	<.001	1.440	1.361–1.524	<.001
Primary site						
Bronchus vs upper lobe	1.116	0.888–1.402	.348	1.314	0.944–1.829	.105
Middle lobe vs upper lobe	1.018	0.944–1.097	.646	1.036	0.918–1.169	.569
Lower lobe vs upper lobe	1.096	1.060–1.134	<.001	1.097	1.038–1.159	.001
Lung/Bronchus overlap vs upper lobe	0.872	0.916–1.234	.439	0.917	0.531–1.583	.756
Tumor laterality (left vs right)	1.010	0.978–1.043	.483			

Statistically significant *P* values are bold.

Abbreviations: HR; hazard ratio; metro, metropolitan area; SBRT, stereotactic body radiation therapy; TAPs, thermal ablative procedures.

eTable 4. Matching Completeness and Goodness of Matches Across Propensity-Matching Models

Algorithm	Matching Completeness	Example of Corrected Patient Characteristics After Matching		Goodness of Matches	
	TAPs Cases n (% matched)	Age of TAPs Patients, y Median (mean)	Age of SBRT Patients, y Median (mean)	Average Difference in Propensity Scores	Absolute Difference in Propensity Scores
Unmatched	1,009	74.0 (73.3)	75.0 (74.4)		
8-digit	80 (7.9%)	76.0 (75.6)	76.0 (75.5)	1.6E-11	1.3E-9
8→7	97 (9.6%)	76.0 (75.6)	75.0 (74.7)	6.3E-9	6.1E-7
8→6	222 (22.0%)	76.0 (74.8)	75.0 (74.7)	2.2E-7	5.0E-5
8→5	620 (61.4%)	75.0 (74.0)	75.0 (74.6)	2.6E-6	1.6E-3
8→4	853 (84.5%)	75.0 (73.8)	75.0 (74.4)	1.2E-5	1.0E-2
8→3	956 (94.7%)	75.0 (73.7)	75.0 (74.2)	5.2E-5	5.0E-2
8→1	987 (97.8%)	75.0 (73.7)	75.0 (74.1)	1.6E-4	1.6E-1

Bolded values are statistically significant.

Abbreviations: SBRT, stereotactic body radiation therapy; TAPs, thermal ablative procedures.

eTable 5. Complete Patient Demographics for Propensity-Matched Patients Using the Greedy 8→4 Model

Parameter	SBRT (N=853) n (%)	TAPs (N=853) n (%)	Univariable ^a
			P Value
Median age (IQR), y	75.0 (69–80)	74.0 (68–81)	
Sex			
Male	405 (47.5)	411 (48.2)	
Female	448 (52.5)	442 (51.8)	
Race			
White	754 (88.4)	786 (92.1)	
Black	78 (9.1)	52 (6.1)	
Indian	2 (0.2)	0 (0.0)	
Pacific Islander	6 (0.7)	9 (1.1)	
Other	5 (0.6)	0 (0.0)	
Missing	8 (0.9)	6 (0.7)	
Charlson-Deyo comorbidity score			
0	451 (52.9)	436 (51.1)	
1	267 (31.3)	264 (31.0)	
2	100 (11.7)	112 (13.1)	
≥3	35 (4.1)	41 (4.8)	
Insurance type			
Not insured	7 (0.8)	7 (0.8)	Ref
Private insurance	98 (11.5)	111 (13)	
Medicaid	28 (3.3)	32 (3.8)	
Medicare	683 (80.1)	681 (79.8)	
Other government	29 (3.4)	13 (1.5)	.017
Unknown	8 (0.9)	9 (1.1)	
Income			
<\$38,000	158 (18.5)	156 (18.3)	
\$38,000–\$47,999	210 (24.6)	223 (26.1)	
\$48,000–\$62,999	227 (26.6)	192 (22.5)	
≥\$63,000	255 (29.9)	270 (31.7)	
Unknown	3 (0.4)	12 (1.4)	
Location, population			
≥1 million	422 (49.5)	384 (45.0)	
250,000–1 million	210 (24.6)	189 (22.2)	
Metro with <250,000	67 (7.9)	86 (10.1)	
Urban >20,000, adjacent to metro	46 (5.4)	52 (6.1)	
Urban >20,000, not adjacent to metro	7 (0.8)	7 (0.8)	
Urban 2,500–20,000, adjacent to metro	45 (5.3)	54 (6.3)	
Urban 2,500–20,000, not adjacent to metro	29 (3.4)	23 (2.7)	
Rural <2,5000, adjacent to metro	1 (0.1)	6 (0.7)	
Rural <2,5000, not adjacent to metro	8 (0.9)	8 (0.9)	
Unknown	18 (2.1)	44 (5.2)	

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Statistically significant *P* values are bold.

Abbreviations: IQR, interquartile range; metro, metropolitan area; NA, not available; NOS, not otherwise specified; SBRT, stereotactic body radiation therapy; TAPs, thermal ablative procedures.

^aEnd point: receipt of SBRT.

eTable 5. Complete Patient Demographics for Propensity-Matched Patients Using the Greedy 8→4 Model (cont.)

Parameter	SBRT (N=853) n (%)	TAPs (N=853) n (%)	Univariable ^a P Value
Residents in ZIP code without high school diploma			
≥29%	133 (15.6)	108 (12.7)	
20%–28.9%	221 (25.9)	220 (25.8)	
14%–19.9%	303 (35.5)	318 (37.3)	
<14%	193 (22.6)	196 (23.0)	
Unknown	3 (0.4)	11 (1.3)	
Facility type			
Academic institute	410 (48.1)	398 (46.7)	
Community cancer program	45 (5.3)	43 (5.0)	
Comprehensive community cancer program	287 (33.6)	299 (35.1)	
Integrated network cancer program	111 (13.0)	113 (13.2)	
Unknown	—	—	
Facility location			
New England	89 (10.4)	80 (9.4)	
Middle Atlantic	174 (20.4)	180 (21.1)	
South Atlantic	161 (18.9)	179 (21.0)	
East North Central	183 (21.5)	172 (20.2)	
East South Central	45 (5.3)	56 (6.6)	
West North Central	52 (6.1)	43 (5.0)	
West South Central	69 (8.1)	66 (7.7)	
Mountain	33 (3.9)	27 (3.2)	
Pacific	47 (5.5)	50 (5.9)	
Unknown	—	—	
Median distance to treating facility (IQR), mi	11.3 (4.9–28.9)	10.8 (4.7–26.6)	
Histology			
Squamous	264 (30.9)	293 (34.3)	
Adenocarcinoma	405 (47.5)	362 (42.5)	
Non–small cell NOS	113 (13.2)	122 (14.3)	
Other	71 (8.4)	76 (8.9)	
Median year of diagnosis (IQR)	2012 (2010–2013)	2010 (2008–2012)	
Median tumor size (IQR), mm	21 (15–29)	18 (14–25)	<.001
Clinical stage			
IA	680 (79.7)	682 (80.0)	
IB	122 (14.3)	126 (14.8)	
“I” NOS	51 (6.0)	45 (5.3)	

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Statistically significant *P* values are bold.

Abbreviations: IQR, interquartile range; metro, metropolitan area; NA, not available; NOS, not otherwise specified; SBRT, stereotactic body radiation therapy; TAPs, thermal ablative procedures.

^aEnd point: receipt of SBRT.

eTable 5. Complete Patient Demographics for Propensity-Matched Patients Using the Greedy 8→4 Model (cont.)

Parameter	SBRT (N=853) n (%)	TAPs (N=853) n (%)	Univariable ^a
			P Value
Tumor grade			
1	81 (9.5)	74 (8.7)	
2	148 (17.4)	162 (19.0)	
3	171 (20.0)	159 (18.6)	
4	2 (0.2)	5 (0.6)	
Unknown	451 (52.9)	453 (53.1)	
Primary site			
Upper lobe	528 (61.9)	480 (56.3)	Ref
Bronchus	3 (0.4)	33 (3.9)	<.0001
Middle lobe	41 (4.8)	30 (3.5)	.004
Lower lobe	261 (30.6)	288 (33.8)	.036
Lung/Bronchus overlap	—	—	
Unknown	20 (2.3)	22 (2.5)	
Tumor laterality			
Right	457 (53.6)	453 (53.1)	
Left	391 (45.8)	366 (42.9)	
Unknown/NA	5 (0.6)	34 (4.0)	

Statistically significant *P* values are bold.

Abbreviations: IQR, interquartile range; metro, metropolitan area; NA, not available; NOS, not otherwise specified; SBRT, stereotactic body radiation therapy; TAPs, thermal ablative procedures.

^aEnd point: receipt of SBRT.

eTable 6. Cox Proportional Analysis for Hazard of Death for Propensity-Matched Patients Using the Greedy 8→4 Model

Parameter	Univariable			Multivariable		
	HR	95% CI	P Value	HR	95% CI	P Value
Treatment (TAPs vs SBRT)	1.270	1.085–1.486	.003	1.265	1.062–1.506	.008
Age (continuous)	1.021	1.007–1.035	.003	1.024	1.009–1.040	.002
Sex (female vs male)	0.696	0.551–0.879	.002			
Charlson-Deyo comorbidity score (3 vs 0)	2.612	1.486–4.592	<.001	3.067	1.655–5.684	<.001
Facility location						
Middle Atlantic vs New England	0.534	0.325–0.877	.013			
South Atlantic vs New England	0.592	0.359–0.976	.040			
Pacific vs New England	0.370	0.187–0.733	.004			
Histology						
Adenocarcinoma vs squamous	0.670	0.506–0.888	.005			
Non–small cell NOS vs squamous	0.539	0.340–0.852	.008			
Tumor grade						
2 vs 1	3.295	1.903–5.703	<.001			
3 vs 1	2.362	1.389–4.016	.002			
Tumor size (continuous)	1.028	1.015–1.041	<.001			
Clinical stage (IB vs IA)	2.421	1.705–3.440	<.001	2.218	1.518–3.241	<.001

Statistically significant *P* values are bold.

Abbreviations: HR, hazard ratio; NOS, not otherwise specified; SBRT, stereotactic body radiation therapy; TAPs, thermal ablative procedures.

eTable 7. OS of SBRT vs TAPs Cohorts Across Matching Models

Model	mOS (mo)		1-y OS (%)		2-y OS (%)		5-y OS (%)	
	SBRT	TAPs	SBRT	TAPs	SBRT	TAPs	SBRT	TAPs
Unmatched	37.7	33.5	86.7	83.1	67.5	62.7	30.6	26.9
8→1	39.8	33.4	88.5	82.8	69.3	62.4	33.7	26.1
8→4	40.4	33.4	89.0	82.9	69.7	62.7	34.4	26.4
8→5	40.4	34.2	88.1	82.0	69.1	63.1	33.7	29.2

Abbreviations: mOS, median overall survival; OS, overall survival; SBRT, stereotactic body radiation therapy; TAPs, thermal ablative procedures.