Stereotactic Body Radiotherapy for Early-Stage Multiple Primary Lung Cancers

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Abstract

Outcomes of patients with early-stage multiple primary lung cancers (MPLC) were reviewed from a prospective database at a high-volume institution. Compared to patients receiving a single course of stereotactic body radiotherapy (SBRT), MPLC patients receiving multiple courses of SBRT or receiving surgery followed by SBRT had no significant detriment in survival, freedom from disease progression, or toxicity.

Background: Patients with multiple primary lung cancers increasingly receive multiple courses of stereotactic body radiotherapy (SBRT). We aimed to clarify the efficacy and safety of such treatments. **Patients and Methods:** We reviewed a prospective lung SBRT database of patients treated for stage I non–small-cell lung cancer between June 2004 and December 2015. **Results:** A total of 374 patients received a single course of SBRT, 14 received synchronous SBRT, 48 received metachronous SBRT alone, and 108 received surgery and metachronous SBRT. Median follow-up was 37.0 months for survivors. Patients who received a single course had a 3-year overall survival (OS) of 54.2% (95% confidence interval [CI], 48.8-59.3), 3-year freedom from progression (FFP) of 67.3% (95% CI, 60.9-72.9), and grade 3 or higher toxicity of 3.5%. Compared to single-course patients, patients receiving metachronous SBRT alone and patients receiving surgery and metachronous SBRT had improved OS (79.7% [95% CI, 64.4-88.9%], $P < .0001$ and 95.4% [95% CI, 89.2-98.0%], $P < .0001$, respectively) and FFP (85.8% [95% CI, 70.7-93.5], $P = .03$ and 95.4% [95% CI, 89.2-98.0%], $P < .0001$, respectively). Patients receiving synchronous SBRT had similar OS (46.4% [95% CI, 19.3-69.9%], $P = .75$) and similar FFP (57.5% [95% CI, 25.3-80.0%], $P = .17$) as single-course patients. There were no significant differences in rates of grade 3 or higher toxicity or of grade 1 or higher toxicity between single-course patients and the other groups. **Conclusion:** Patients who received either synchronous or metachronous SBRT had no significant detriment in OS or toxicity compared to single-course patients. This supports the use of SBRT in patients with multiple primary lung cancers.

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Introduction

Lung cancer remains the leading cause of cancer mortality in the United States and abroad, with non–small-cell lung cancer (NSCLC) comprising 85% of all cases.[1] As a result, there have been efforts supported by the US Preventive Services Task Force to diagnose lung cancers at earlier and more treatable stages using annual low-dose computed tomography (CT) for at-risk populations.[2] These screening efforts are part of the reason why up to 30% of lung cancer cases in the United States are now being diagnosed at an early stage, defined as either stage I or II.[3] These early tumors can be successfully resected, with local control rates of up to 96% and overall survival (OS) rates of approximately 50% to 60% at 3 years.[4] A significant obstacle to treating these patients is that many of them have underlying pulmonary or cardiac comorbidities that make them poor candidates for surgery.[5] Fortunately, stereotactic body radiotherapy (SBRT) has emerged as an effective treatment modality for patients with medically inoperable, early-stage NSCLC, achieving local control rates similar to those of surgery.[5]

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Current literature regarding disease control and treatment toxicity of SBRT has largely been limited to patients with a single early-stage NSCLC. However, patients with medically inoperable disease who are diagnosed with multiple simultaneous tumors may need to receive parallel courses of SBRT (synchronous treatment). Likewise, patients with medically inoperable disease who develop new primary tumors after initial treatment may need additional courses of SBRT (metachronous treatment).

The efficacy and safety of SBRT for patients with synchronous and metachronous early-stage NSCLC is not well defined. Therefore, we retrospectively analyzed the clinical outcomes of this cohort of patients at our institution with high volumes of prior surgical patients. In contrast to other reports on multiple primary lung cancers (MPLC), we compare these MPLC clinical outcomes to those of patients treated with SBRT for a single early-stage NSCLC at our institution.

Patients and Methods

Eligibility Criteria

An institutional review board—approved prospective lung SBRT database was retrospectively analyzed for patients who were first treated with SBRT between June 2004 and December 2015 in the Department of Radiation Oncology at Washington University in St Louis. All patients provided written informed consent for inclusion in this database before receiving treatment.

The selection criteria for this study were as follows: American Joint Committee on Cancer 7th edition stage IA or IB NSCLC confirmed by pathology, or clinically diagnosed by positron emission tomography (PET) and CT findings, if biopsy was deemed unsafe; free from any other malignancies or metastases at the time of SBRT administration; received definitive-intent treatment; at least 3 months of follow-up after SBRT including at least one imaging study (either PET or CT scan) to assess response to therapy; and must not have received prior conventionally fractionated thoracic radiation.

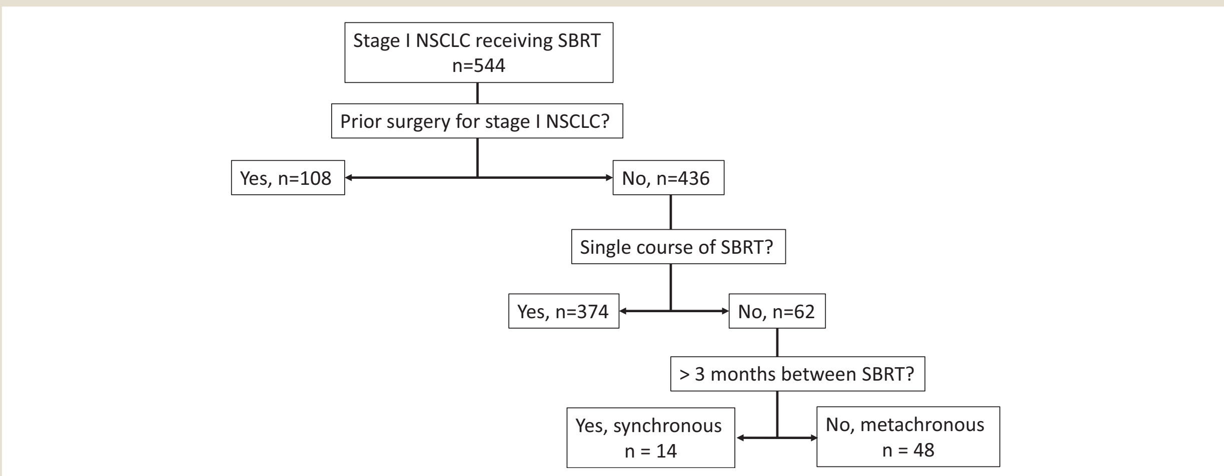
Eligible patients were then separated according to whether they received SBRT alone or if they underwent surgery first, then SBRT. Patients who received SBRT alone were then separated according to whether they were treated with a single course, a synchronous course, or a metachronous course of SBRT. Metachronous SBRT courses were defined as treatments more than 3 months apart (Figure 1).

Treatment Methods

SBRT planning was performed as previously described.[6] Patients were immobilized either by the Elekta Stereotactic Body Frame (Elekta, Crawley, England, UK), the BodyFix system (Medical Intelligence, Munich, Germany), or the Alpha Cradle (Smithers Medical Products, North Canton, OH). To characterize tumor motion, patients underwent simulation using 4-dimensional CT, which was performed using a 16-slice CT (Somatom Sensation 16; Philips Medical, Cleveland, OH). If 4-dimensional CT showed tumor movement of > 10 mm in any direction, abdominal compression was used in addition to the above immobilization techniques. Patients immobilized by the BodyFix system additionally received 2 thoracic CT scans and a helical CT scan. Patients immobilized with the Elekta Stereotactic Body Frame additionally received a helical CT of the thorax.

SBRT delivery was performed as previously described.[6,7] Maximum intensity projections were used to set the internal target volume for the tumor and its path of motion. Planning target volume was set as 5 mm around the border of the internal target volume. Radiotherapy was generally delivered using a 7-11 noncoplanar beam arrangement. Superposition/convolution algorithms were used to correct for heterogeneity. Dose was delivered to ≥ 95% of the planning target volume and was most commonly set to the 75% to 85% isodose line (range, 60-90% isodose line). Patients either received 5400 cGy in 3 fractions for peripheral lesions or 5000 to 5500 cGy in 5 fractions for tumors that were within 2 cm of the proximal bronchial tree or were adjacent to the mediastinal or

Figure 1 CONSORT Diagram



Abbreviation: CONSORT = Consolidated Standards of Reporting Trials.

pericardial pleura. The standards set in RTOG 0813[8] and RTOG 0236[9] were used for normal tissue dose limits.

Follow-up

Follow-up consisted of physical examination and volumetric imaging with CT or PET/CT every 3 to 4 months after completion of therapy for the first 2 years, then every 6 months thereafter. If there was clinical suspicion for local, regional, or metastatic disease, patients underwent repeat assessment and evaluation similar to that at initial diagnosis.

Evaluation

OS was calculated starting from the diagnosis date of the first NSCLC. The diagnosis dates were defined as the earliest conclusive biopsy results or PET scans. Freedom from progression (FFP) and local control were calculated starting from the date of the first surgery or SBRT fraction. Progression was defined as any primary tumor site, regional, or distant progression, identified either through CT or PET scan, that occurred after the completion of SBRT. If only one new lesion in the lungs was seen on CT imaging at a follow-up, it was defined as a new primary lesion. If more than one lesion in the lungs was seen, it was defined as metastatic disease. Patients were censored if they died, but this was not counted as treatment failure. Local failure was defined as any in-field progression that occurred after the completion of SBRT, identified by PET scan. It was assessed for each individual tumor treated with SBRT. Toxicity was assessed according to the Common Terminology Criteria for Adverse Events, version 4.0.[10] This assessment was generally performed prospectively by the treating physician. In cases where no grade was assigned, this was done by retrospectively interpreting the physician's notes. Severe toxicity was defined as adverse events that were grade 3 or higher.

Statistical Analysis

All statistical comparisons were made between the group of patients who received a single course of SBRT and each of the other 3 treatment groups. Differences in baseline patient characteristics were assessed by the Fisher exact test for gender, Eastern Cooperative Oncology Group (ECOG) performance status, percentage of patients who have ever smoked, and percentage of tumors that were sampled by biopsy. The Wilcoxon rank-sum test was used for the other patient characteristics. Cumulative rates of OS, FFP, local control, and toxicity were calculated by Kaplan-Meier survival analysis. Significance was calculated by a Wilcoxon test. The differences in severe toxicity and overall toxicity were assessed by 2-tailed Fisher exact tests. Values of $P < .05$ were considered

Table 1 Patient Characteristics at Diagnosis

	Single	Synchronous		Metachronous		Surgery + SBRT	
Characteristic	**Value**	**Value**	***P***	**Value**	***P***	**Value**	***P***
No. of patients	374	14	—	48	—	108	—
Age at diagnosis (years) (mean)	73.7	73.4	.85	72.9	.44	70.6	< .01*
Gender							
Male	49.0%	14.3%		56.3%		34.3%	
Female	51.0%	85.7%	.01*	43.7%	.36	65.7%	.01*
Smoking history (pack-years) (mean)	52.4	58.0	.53	51.0	.94	57.3	.18
Have Ever Smoked?							
Yes	93.6%	100%		97.9%		94.4%	
No	6.4%	0%	1.00	2.1%	.34	5.6%	1.00
ECOG Performance Status							
0	24.6%	7.7%		41.3%		36.5%	
1	55.0%	84.6%	.15	47.8%		51.4%	
2	20.4%	7.7%		10.9%	.04*	12.2%	.02*
Age-adjusted Charlson Comorbidity Score (mean)	5.4	5.8	.35	5.3	.68	5.8	< .01*
Follow-up duration (months) (mean)	27.7	22.7	.37	44.3	< .0001*	38.7	< .0001*
Tumor Location			1.00		.54		.57
Central	16.8%	14.3%		12.5%		19.4%	
Peripheral	83.2%	85.7%		87.5%		80.6%	
Biopsy Performed			.23		.66		< .0001*
Yes	85.6%	100%		89.6%		62.0%	
No	14.4%	0%		10.4%		38.0%	

Pairwise comparisons were made between single SBRT treatment group and each of other 3 groups by Fisher exact test or 2-sided Wilcoxon test.
Abbreviations: ECOG = Eastern Cooperative Oncology Group; SBRT = stereotactic body radiotherapy.
*Statistically according ($P < .05$).

Table 2 Clinical Outcomes

Outcome	Single SBRT	95% CI	Synchronous SBRT	95% CI	Metachronous SBRT	95% CI	Surgery + SBRT	95% CI
3-year OS rate	54.2%	48.8-59.3%	46.4%	19.3-69.9%	79.7%*	64.4-88.9%	95.4%*	89.2-98.0%
3-year FFP rate	67.3%	60.9-72.9%	57.5%	25.3-80.0%	85.8%	70.7-93.5%	95.4%*	89.2-98.0%
3-year local control rate	89.4%	85.3-93.5%	75.0%	53.8-96.2%	96.0%	90.3-100%	98.2%*	95.8—100%

Abbreviations: CI = confidence interval; FFP = freedom from progression; OS = overall survival; SBRT = stereotactic body radiotherapy.
*Statistically significant difference compared to single SBRT cohort.

statistically significant. The PHREG procedure was used for the multivariate analysis of the differences in OS and FFP intervals seen between the groups. All statistical analyses were performed by SPSS Statistics 24 (IBM, Armonk, NY) and SAS 9.4 (SAS Institute, Cary, NC).

Results

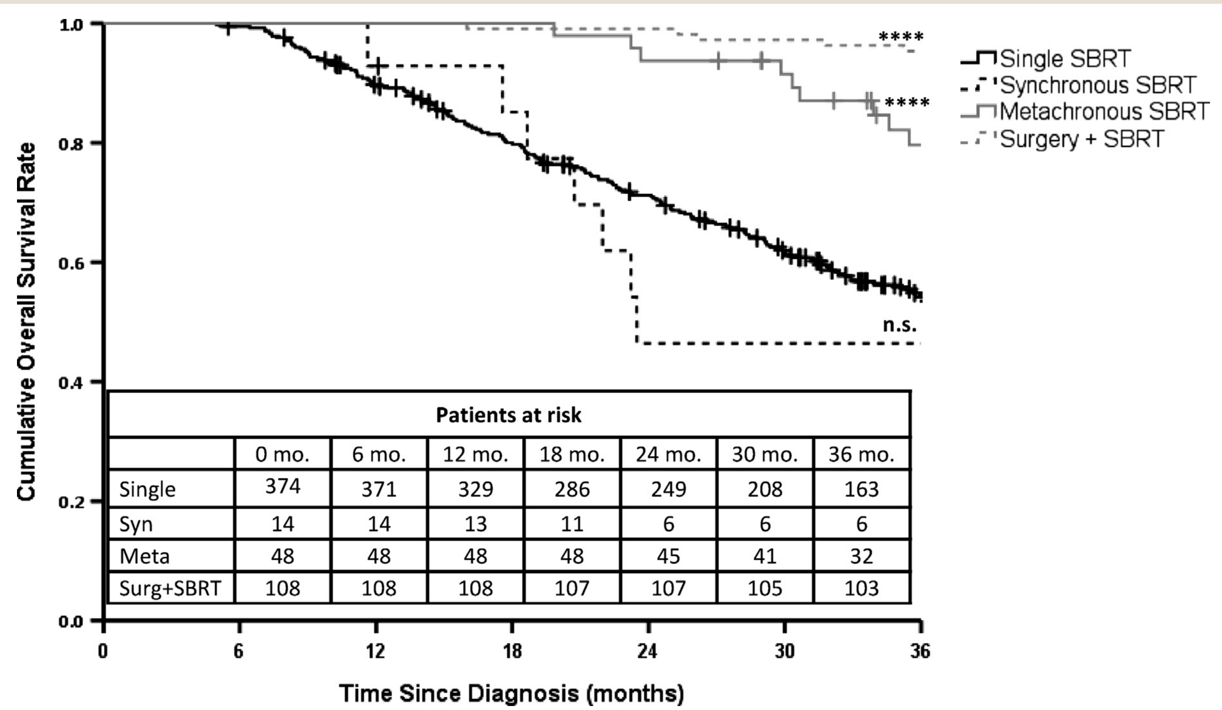
Characteristics

Table 1 shows the characteristics of the 544 eligible patients. A total of 374 patients were treated with a single course of SBRT, 14 patients were treated with synchronous courses of SBRT, 48 patients were treated with metachronous courses of SBRT alone, and 108 patients were treated first with surgery for at least one tumor and then with metachronous SBRT for at least another tumor (Figure 1). Median follow-up time for the entire cohort was 26.7 months (range, 3-152 months) and 37 months for survivors (range, 3-153 months). Women comprised 54% of the patients. Median age at the time of first diagnosis was 73 (interquartile range, 67-79 years), and median age-adjusted Charlson comorbidity score was 5 (interquartile range, 4-7). Compared to patients who received SBRT for a single lesion, patients treated with metachronous SBRT alone ($P = .04$) or both surgery and metachronous SBRT ($P = .02$) had significantly better ECOG performance scores. Meanwhile, there was no statistical difference in performance scores between single treatment or synchronous SBRT patients ($P = .15$).

Clinical Outcomes

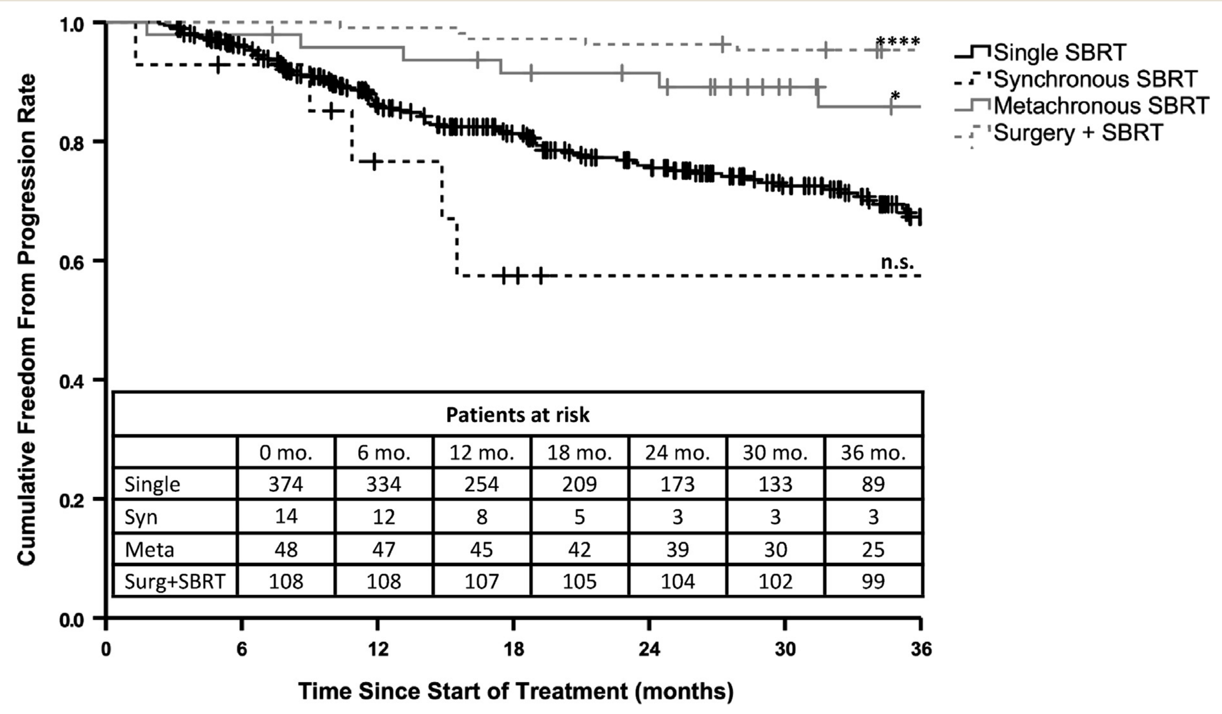
Three-year OS, FFP, and local control rates and their 95% confidence intervals are listed in Table 2. Compared to patients who received a single course of SBRT, patients who received metachronous courses of SBRT alone ($P < .0001$) and patients who received both surgery and metachronous SBRT ($P < .0001$) had

Figure 2 Overall Survival for Each Group. Kaplan-Meier Survival Analysis was Performed, Followed by Wilcoxon Tests Comparing Each Group to Single SBRT Treatment Group. ****$P < .0001$



Abbreviations: n.s. = not significant; SBRT = stereotactic body radiotherapy.

Figure 3 Freedom From Progression for Each Group. Kaplan-Meier Survival Analysis was Performed, Followed by Wilcoxon Tests Comparing Each Group to Single SBRT Treatment Group. *$P < .05$, ****$P < .0001$



	0 mo.	6 mo.	12 mo.	18 mo.	24 mo.	30 mo.	36 mo.
Single	374	334	254	209	173	133	89
Syn	14	12	8	5	3	3	3
Meta	48	47	45	42	39	30	25
Surg+SBRT	108	108	107	105	104	102	99

Abbreviations: n.s. = not significant; SBRT = stereotactic body radiotherapy.

significantly higher OS. There was no significant decrease in OS for patients who received synchronous courses of SBRT ($P = .75$; Figure 2). Patients who received synchronous courses of SBRT had no significant difference in FFP compared to patients who received a single course of SBRT ($P = .17$). However, there was a significant increase in FFP in patients who received both surgery and metachronous SBRT ($P < .0001$) and in patients who received metachronous courses of SBRT alone ($P = .03$; Figure 3). Compared to patients who received a single course of SBRT, there appeared to be a decrease in local control for patients who received synchronous SBRT treatments ($P = .06$). However, there was an increase in patients who received metachronous SBRT ($P = .10$) and a statistically significant increase in patients who received both surgery and SBRT ($P = .007$; Figure 4).

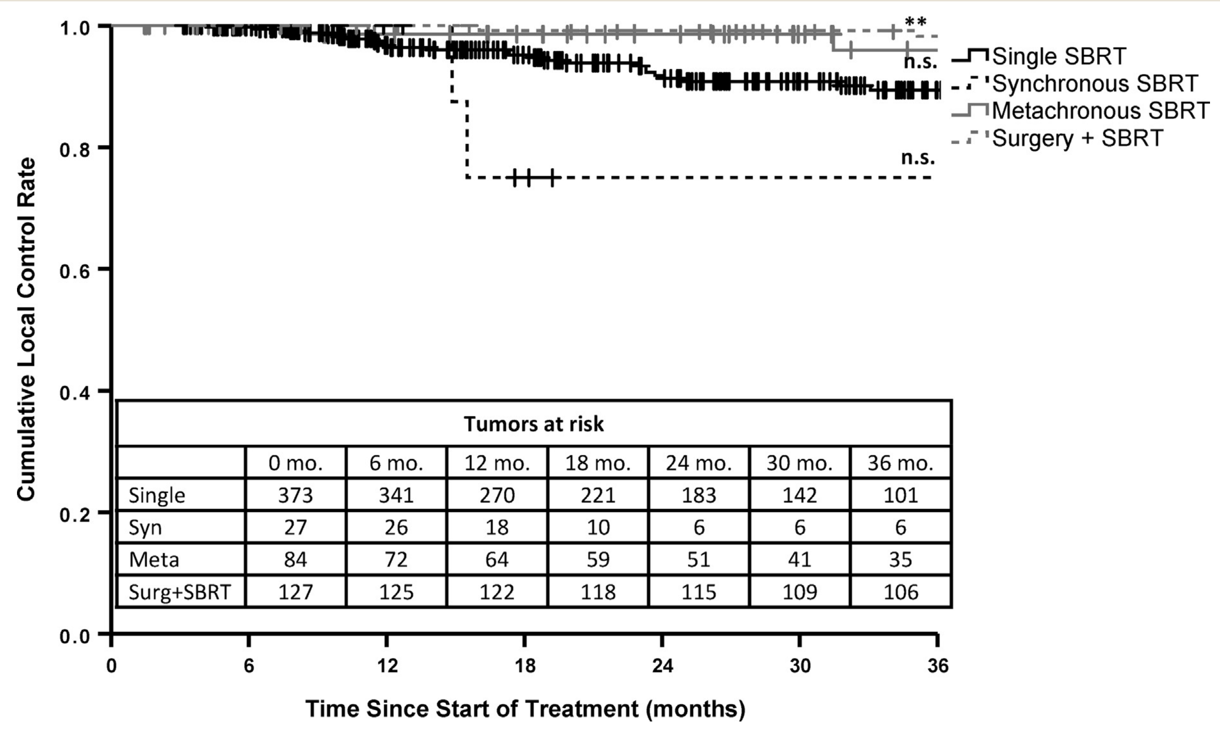
When only patients with at least 1 year of follow-up were included in the analysis, patients who received a metachronous course of SBRT ($P = .006$) or both surgery and metachronous SBRT ($P < .001$) continued to have significantly higher OS, while synchronous patients still did not have significantly decreased OS ($P = .30$). For FFP, the only significant change was that the higher FFP in the metachronous group was no longer statistically significant ($P = .17$) compared to the single treatment group. For local control, the only significant change was that the decrease seen in the synchronous group became statistically significant ($P < .001$) despite the 3-year local control rate staying at 75.0%.

Multivariate analysis was performed to look for the patient characteristics that predicted OS and FFP interval lengths. The statistically significant patient attributes in order of decreasing significance were type of tumor (ie, single, synchronous, metachronous) ($P < .0001$), ECOG ($P < .0001$), gender ($P = .008$), and central location ($P = .03$). For FFP, the only statistically significant attribute was type of tumor ($P < .0001$).

Toxicity

The severe (grade 3 or higher) toxicity rate for patients treated with SBRT for single lesions was 3.5%, and the overall (any grade) toxicity rate was 29.4%. There was no significant difference in severe or overall toxicity rates for patients treated with synchronous SBRT, who had rates of 14.3% ($P = .10$) and 50% ($P = .14$), respectively. Likewise, there was no significant difference in severe or overall toxicity rates for patients treated with metachronous SBRT alone, who had rates of 4.2% ($P = .68$) and 37.5% ($P = .24$), respectively, or for patients treated with surgery and metachronous SBRT, who had rates of 5.6% ($P = .40$) and 33.3% ($P = .48$), respectively. There were 2 total cases of grade 5 toxicities, which consisted of 1 case of hemoptysis in a patient treated with SBRT for a single lesion and 1 case of pneumonitis in a patient treated with SBRT alone for metachronous lesions (Table 3). When Kaplan-Meier analysis was performed for the separate incidences of radiation pneumonitis or chest wall toxicity, there were no

Figure 4 Local Control for Tumors Treated With SBRT in Each Group. Kaplan-Meier Survival Analysis was Performed, Followed by Wilcoxon Tests Comparing Each Group to Single SBRT Treatment Group. **$P < .01$



	0 mo.	6 mo.	12 mo.	18 mo.	24 mo.	30 mo.	36 mo.
Single	373	341	270	221	183	142	101
Syn	27	26	18	10	6	6	6
Meta	84	72	64	59	51	41	35
Surg+SBRT	127	125	122	118	115	109	106

Abbreviations: n.s. = not significant; SBRT = stereotactic body radiotherapy.

significant differences between the single treatment group and the other 3 groups (Figure 5).

Discussion

For patients with a single stage I NSCLC lesion, SBRT and surgery appear to achieve similar OS rates.[4,11-14] However, for patients who have either synchronous or metachronous MPLC, the results have been less encouraging for SBRT. Chang et al[15] studied a sample of 39 synchronous MPLC patients and 62 metachronous MPLC patients and found that synchronous SBRT achieved a significantly lower 4-year OS rate compared to metachronous SBRT (39.7% vs. 52.7%) and a significantly lower 4-year progression-free survival (PFS) rate (30.4% vs. 75.6%). Although Chang et al did not define PFS, it is likely similar to our use of FFP. The PFS rate was numerically larger than the OS rate in their synchronous cohort, which means that they also censored patients who were deceased in their PFS analysis. These authors also provided 7 fractions of 10 Gy for each SBRT procedure, while we limited SBRT to 5 fractions. Likewise, a study by Creach et al[7] used a sample of 15 synchronous patients and 48 metachronous patients and found that the 2-year OS rate was significantly lower for the synchronous group than for the metachronous group (27.5% vs. 68.1%), as was the 2-year PFS rate (0 vs. 53.3%). This current reports defines synchronous as treatment within 3 months, while the report of Creach et al defined synchronous for any patient where 2 pulmonary nodules existed simultaneously. These earlier studies by Chang et al and Creach et al demonstrate that while SBRT is effective for treating metachronous primary lung cancers, it is less effective for treating synchronous cancers, thus posing a therapeutic challenge. In contrast to Chang et al and Creach et al, our results support the idea that SBRT can be effective for treating synchronous lung lesions. We found that our small synchronous SBRT had no significant difference in 3-year OS (46% vs. 54%, $P = .75$) and only had a modest decrease in 3-year local control (75% vs. 89%, $P = .18$) compared to the single treatment group.

There have been a few studies that combined synchronous primary lung cancer patients who received SBRT with those who received a combination of surgery and SBRT to achieve a higher sample size. However, they did not compare these 2 subgroups to each other to assess their relative efficacy. Shintani et al[16] studied 18 patients and found a 3-year OS rate of 69.1% and a PFS rate of 43.2%. Griffioen et al[17] sampled 62 patients and found a 2-year OS rate of 56% and a PFS rate of 87%. Griffioen et al likewise did not explicitly define PFS, but because it is larger than their OS rate, it is likely comparable to our definition of FFP. Both sets of authors concluded that synchronous treatments of SBRT were effective, which supports our conclusion that SBRT serves as an effective treatment for synchronous primary lung cancers.

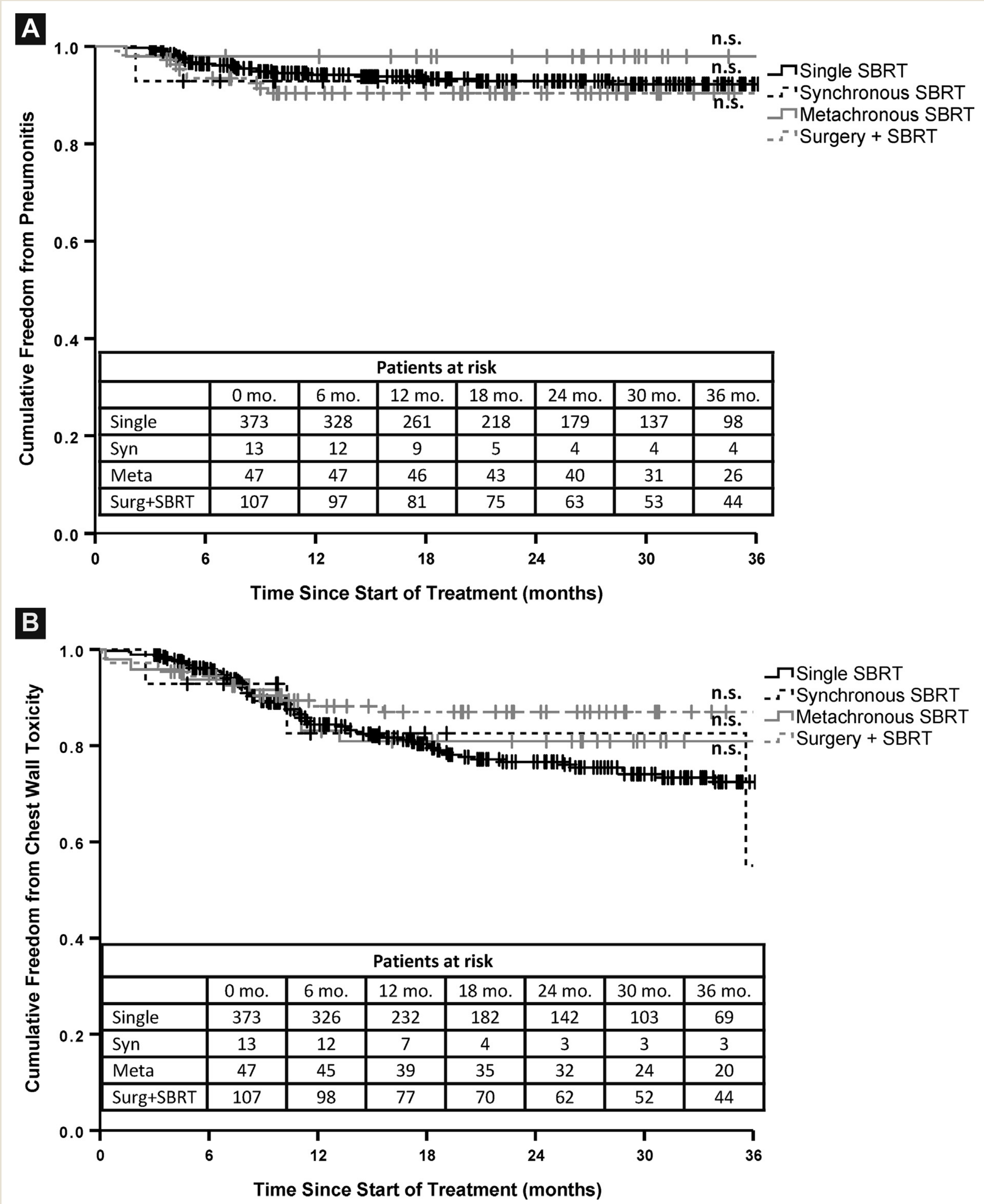
A few studies have instead chosen to combine synchronous and metachronous SBRT patients into a single group, and they have shown more favorable results for treating synchronous or metachronous MPLC. Using a sample of 63 MPLC patients, Owen

Table 3 SBRT-Related Toxicity in Each Group

Type of Toxicity	Single (N = 374)					Synchronous (N = 14)					Metachronous (N = 48)					SBRT + Surgery (N = 108)				
	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
Chest wall	39	36	2	1		1	3				11	3				15	3	1		
Pneumonitis	7	12	4				1	1				1	1		1		10	4		
Brachial plexopathy		2										1					1			
Bronchial obstruction			3														1			
Dermatitis	5	4	1			1						1				2			1	
Esophagitis		1						1			1	2								
Hemoptysis					1															
Pleural effusion			2									1								
Other	1	3									1									
Severe (Grade 3 or Higher)	14					2					2					6				
%	3.5					14.3					4.2					5.6				
Significance	—						NS				NS					NS				
P	—					.10					.68					.40				
Overall	124					8					24					38				
% of patients	29.4					50					37.5					33.3				
Significance	—					NS					NS					NS				
P	—					.14					.24					.48				

Numbers 1 to 5 indicate grade. Toxicities were graded according to Common Terminology Criteria for Adverse Events. Analysis was performed by 2-sided Fisher exact tests between single treatment group and each of other 3 groups.
Abbreviations: NS = not significant; SBRT = stereotactic body radiotherapy.

Figure 5 Freedom From Pneumonitis (A) and Chest Wall Toxicity (B). Kaplan-Meier Survival Analysis was Performed, Followed by Wilcoxon Tests Comparing Each Group to Single SBRT Treatment Group



Abbreviations: n.s. = not significant; SBRT = stereotactic body radiotherapy.

et al[18] found that SBRT resulted in a 1-year OS rate of 85% and a 1-year PFS rate of 91.9%. Because their PFS is larger than OS, it is more comparable to our definition of FFP. Matthiesen et al[19] had a sample of 10 patients and found that 6 of 10 patients were alive and 20 of 21 tumors were locally controlled at a median follow-up time of 15.5 months. However, a limitation of these studies is that most of their patients received metachronous SBRT. Therefore, these survival statistics likely represent the metachronous and not the synchronous group. Taking this into consideration, these 2 studies confirm our findings about metachronous primary lung cancers. Our study showed that metachronous SBRT treatment had significantly higher 3-year OS (79.7% vs. 54.2%, $P < .0001$) and a similar 3-year local control rate (94.5% vs. 89.4%, $P = .24$) compared to single SBRT treatments.

We believe that our metachronous SBRT treatment group had a significantly higher OS than our single SBRT treatment group because of the immortal time bias. Patients who have a shorter life expectancy with more comorbid diseases are less likely to manifest metachronous disease. Therefore, patients who do manifest metachronous disease will tend to have a longer expected life span. Similarly, we found that patients who received both surgery and metachronous SBRT also had a higher OS rate. This likely occurred because patients eligible for surgery, as opposed to SBRT, tend to be healthier and have fewer comorbidities, which gives them a longer life expectancy. The baseline patient characteristics of this study support this hypothesis, with both of these groups having significantly better ECOG performance status scores compared to the single treatment group (Table 1). Our multivariate analysis supports this because the type of treatment group the patients were part of was the most important predictor of both OS and FFP. Being able to receive metachronous SBRT or qualifying for surgery appears to confer certain survival and FFP benefits—and is even more important than age at diagnosis, ECOG performance status, or tumor location.

As for the safety of multiple courses of SBRT, we found that for both severe adverse events (grade 3 or higher) and all adverse events, there was no significant difference in the toxicity rates between the single treatment group and the other 3 MPLC groups. Repeating the statistical tests with Kaplan-Meier survival analysis also failed to show statistically significant differences between the single treatment group and any of the other 3 groups. This suggests that multiple courses of radiotherapy are well tolerated by patients, without worrisome increases in radiation pneumonitis, dermatitis, or chest wall toxicity.

Our study has some limitations. First, as was previously mentioned, is the smaller sample size for the synchronous treatment group. Another limitation is that not all patients underwent biopsy. This was generally because of an increased risk for complications due to pulmonary comorbidities. A third limitation was that the toxicity data used in this study were physician reported and in some cases assessed retrospectively. A more robust means of toxicity assessment would include consistent use of validated instruments as well as patient-reported outcomes. A final limitation is that the study is retrospective in nature and is therefore subject to inherent bias. However, despite these limitations, our results confirm previously published reports and serve as a basis for future, larger multi-institutional studies.

In conclusion, SBRT appears effective and safe for patients with for synchronous and metachronous MPLC. However, despite these results, further study and validation against other institutional experiences merit examination.

Clinical Practice Points

- Smaller retrospective series of patients with multiple, early-stage lung cancers (MPLC) receiving SBRT have been published with differing outcomes.
- This is the first study to compare outcomes of these patients with MPLC directly with those receiving SBRT for a single early-stage lung cancer. It did so from a prospective database at a high-volume institution.
- This study is also notable as one of the largest series published to date of previous thoracic surgery followed by SBRT for a second cancer.
- This comparative study with single course SBRT showed no statistically significant increases in toxicity in patients who receive SBRT after previous lung surgery or who receive multiple courses of SBRT, even courses of SBRT within 3 months of each other. This supports as safe the repeated use of SBRT in this population.
- This study suggests improved disease and survival outcomes in patients receiving both surgery and SBRT as well as multiple courses of SBRT alone for MPLC, though this could be due to selection bias.
- In contrast to other studies, we found that the use of SBRT for synchronous MPLC had similar disease outcomes as the use of SBRT for a single lung cancer.
- Together, these data support the use of SBRT for any type of MPLC as both safe and effective.

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Disclosure

The authors have stated that they have no conflict of interest.

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