pISSN 1598-2998, eISSN 2005-9256
https://doi.org/10.4143/crt.2024.1040 Cancer Res Treat. 2025;57(4):1135-1143

Original Article

Stereotactic Ablative Radiotherapy versus Surgery in Patients with Pulmonary Metastases from Colorectal Cancer

Byung Min Lee[1,2], **Ha Eun Kim**[3], **Young Ho Yang**[3], **Seung Yoon Yang**[4], **Han Sang Kim**[5], **Seo Hee Choi**[1], **Woong Sub Koom**[1], **Byung Jo Park**[3], **Jee Suk Chang**[1]

[1]Department of Radiation Oncology, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, [2]Department of Radiation Oncology, Uijeongbu St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, [3]Department of Thoracic and Cardiovascular Surgery, Yonsei University College of Medicine, Seoul, [4]Division of Colon and Rectal Surgery, Department of Surgery, Yonsei University College of Medicine, Seoul, [5]Division of Medical Oncology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea

Purpose We compared the local control rate and toxicity of stereotactic ablative radiotherapy (SABR) versus wedge resection for colorectal pulmonary metastases.

Materials and Methods We retrospectively reviewed medical charts and imaging of patients treated with SABR or wedge resection between 2010 and 2017 at a single institution.

Results A total of 404 patients were treated with local therapy for 528 pulmonary metastatic lesions. While surgery was frequently used upfront for smaller, solitary metastases without other site involvement, SABR was often used for larger, multiple lesions and disease burdens beyond the lungs. The 3-year local control rate was 88.6% following surgery, which was not significantly different from that with SABR at 86.7% (p=0.174). No major postoperative complications or mortality were observed in the surgery group, and 2.8% of patients in the SABR group experienced grade 3-4 radiation pneumonitis.

Conclusion SABR was used in patients with a higher risk of progression compared to those undergoing surgery, yet it has similar local control rates to wedge resection.

Key words Pulmonary metastases, Colorectal neoplasms, Stereotactic ablative radiotherapy, Metastasectomy, Local control

Introduction

The lung is the second most common site for metastases from colorectal cancer [1]. Surgical metastasectomy is the preferred option when complete resection is feasible, and multiple studies have demonstrated promising survival outcomes for selected patients [2]. The increasing prevalence of metastasectomy has been driven by high-volume institutions, where patients experience low postoperative morbidity and mortality rates during inpatient care [3]. Stereotactic ablative radiotherapy (SABR) was initially introduced for medically inoperable patients or those who declined surgical resection [4]. SABR is a non-invasive technique that administers a high dose per fraction, typically in 1-5 sessions, using highly conformal beams to ablate the tumor while minimizing toxic effects to surrounding organs. The use of SABR for oligometastatic disease (OMD) has significantly increased, particularly in centers where surgeons routinely perform metastectomies at their institutions [5].

In patients with colorectal cancer and lung metastases, the PulMiCC trial was the first randomized clinical trial that compared surgical metastasectomy with continued active monitoring [6]. The trial was halted early due to poor and declining recruitment, and the small number of study participants precluded a conclusive analysis. Contrarily, the SABR-COMET trial, a landmark study, showed that SABR improves overall survival (OS) in patients with OMD from various histologies and metastatic sites [7], prompting further research, including histology-specific and phase 3 trials [8]. Since the publication of the SABR-COMET trial results, establishing clinical equipoise has become challenging, which complicates the initiation of similar randomized trials like the PulMiCC trial, particularly in metastatic colorectal cancer (mCRC) where local therapy for liver metastases is already well established [9].

Despite the lack of level I evidence, one of the clinically

Correspondence: Jee Suk Chang
Department of Radiation Oncology, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea
Tel: 82-2-2228-8095 E-mail: changjeesuk@yuhs.ac

Co-correspondence: Byung Jo Park
Department of Thoracic and Cardiovascular Surgery, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea
Tel: 82-2-2228-2140 E-mail: bzpark@yuhs.ac

Received October 29, 2024 **Accepted** February 5, 2025
Published Online February 6, 2025

*Byung Min Lee and Ha Eun Kim contributed equally to this work.

relevant questions in managing lung metastases from mCRC in clinics extends beyond the choice of whether to apply local therapy; it crucially involves selecting the optimal local therapy modality. To date, no completed randomized trials are comparing different local therapy modalities for pulmonary metastases, which leaves a significant gap in evidence-based guidance for treating physicians. Thus, this study aims to compare the effectiveness of SABR versus surgical metastasectomy in terms of local control, oncologic outcomes, and treatment-related toxicity.

Materials and Methods

1. Study patients

Consecutive patients with mCRC treated either with SABR or surgical resection for pulmonary metastases between 2010 and 2017 were included in this retrospective analysis (n=435). Patients who were lost to follow-up before 6 months were excluded from the analysis (n=21), while those who died within 6 months were included. Also, those who received radiation dose less than 100 Gy in biologically effective dose (BED) were excluded (n=10). Totally, 404 patients were included for analysis.

In our institution, patients diagnosed with lung metastases were recommended to be monitored with chest computed tomography (CT) and abdomen-pelvic CT scans, along with tumor marker tests every three months. SABR or metastasectomy for pulmonary metastasis was considered in multidisciplinary discussions. The institutional treatment policy, including the major considerations and indications for SABR and surgery for lung metastases from colorectal cancer, is summarized in Table 1. When newly diagnosed lung metastases were few in number and surgically resectable, discussions primarily revolved around upfront surgical resection. Surgical resection was recommended based on the Thomford criteria [10]. In cases where the metastases were deemed unresectable, upfront systemic therapy was initiated. Upon a favorable response, with the metastases remaining few, the possibility of surgery or SABR was reconsidered. This approach was similarly applied to recurrent lung metastases. Further details on the multidisciplinary approach have been extensively discussed in previous publications [11]. The timing of each treatment is shown in Fig. 1. While the number of procedures in the surgery group fluctuated slightly, there was an overall modest increase during the study period. In contrast, the SABR group showed a clear upward trend, particularly after 2015.

2. Stereotactic ablative radiotherapy

Lung metastases were treated using either volumetric modulated arc therapy or CyberKnife with real-time tumor tracking. A four-dimensional computed tomography simulation was conducted to define the internal target volume (ITV), which incorporated additional 5 mm margins to account for set-up uncertainties, thereby establishing the planning target volume (PTV). In cases where CyberKnife (Accuray Inc.) was used, fiducial placement was followed by the direct setting of the PTV margin of 5 mm from the gross tumor volume without defining an ITV. To manage respiratory motion, vacuum vac-lock systems or body compressors were employed. A full-body vac-lock was utilized for immobilization. Dur-

Table 1. Institutional treatment considerations for surgery and SABR in lung metastases from colorectal cancer

Factor	Surgery (metastasectomy)	SABR
Patient fitness	Good performance status with good pulmonary function	Can be used in patients who refuse surgery, are inoperable, elderly, or have high comorbidities
Disease extent	Primarily for patients with a limited number of lung metastases (e.g., 1-2) and no evidence of metastases in other organs	Often used when slightly more extensive lung metastases are present (e.g., 2-3) or even when extrapulmonary metastases coexist
Tumor location	Preferred for peripheral lung lesions amenable to limited surgical resection (wedge resection)	Can treat both central and peripheral lung lesions, though special consideration is required for central tumors due to higher toxicity risks
Disease timing	Preferred for metachronous lung metastases	More likely used for synchronous metastases
Treatment goal	Curative intent	With the intent to achieve either curative outcomes or to prolong disease control in conjunction with systemic therapy
Patient preference	Patients willing to undergo invasive procedure	Patients preferring non-invasive treatment
Other consideration	Provides definitive pathological confirmation of malignancy	Cannot confirm pathology, so the risk of treating non-malignancy always exists

SABR, stereotactic ablative radiotherapy.

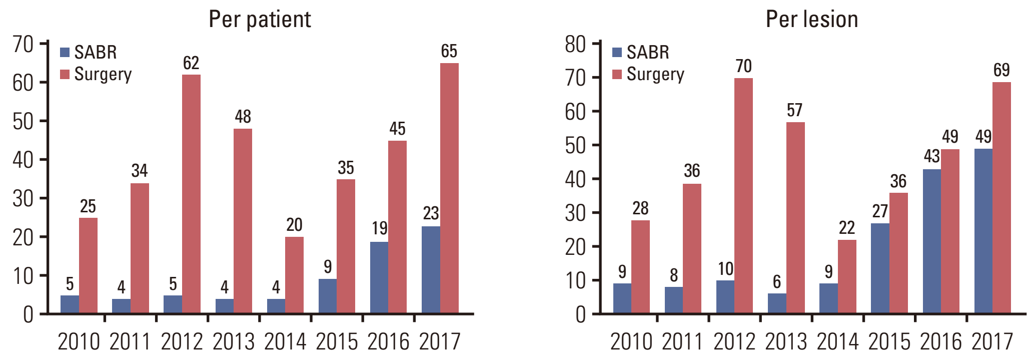

Fig. 1. Timing of local treatment for each patient group. SABR, stereotactic ablative radiotherapy.

Table 2. Baseline characteristics (n=528 lesions in 404 patients)

Variable	Surgery (n=367 lesions in 334 patients)	SABR (n=161 lesions in 70 patients)	p-value
Age (yr)[a)]	59.6±11.7	61.5±12.2	0.258
Sex			
Male	221 (60.2)	82 (50.9)	0.047
Female	146 (39.8)	79 (49.1)	
CCI			
< 2	203 (55.3)	72 (44.7)	0.025
≥ 2	164 (44.7)	89 (55.3)	
Diagnosis-to-treatment interval (mo)	1.8 (0.6-9.0)	14.2 (8.6-32.9)	< 0.001
Tumor size (cm)[a)]	1.5 (1.0-2.5)	1.5 (1.0-4.7)	0.003
Tumor size (cm)[a)]	2.2±1.8	2.8±2.3	0.003
No. of pulmonary metastasis[a)]	1 (1-2)	3 (1-5)	< 0.001
Presence of mediastinal lymph node metastases[a)]			
Yes	14 (3.8)	23 (14.3)	< 0.001
No	353 (96.2)	138 (85.7)	
Presence of extrapulmonary metastases[a)]			
Yes	63 (17.2)	39 (24.2)	0.059
No	304 (82.8)	122 (75.8)	
CEA level (ng/mL)[a)]	3.33 (1.66-7.99)	2.92 (2.09-9.06)	0.716
Bevacizumab-containing chemotherapy			
Yes	171 (46.6)	99 (61.5)	0.002
No	196 (53.4)	62 (38.5)	
Cetuximab-containing chemotherapy			
Yes	58 (15.8)	51 (31.7)	< 0.001
No	309 (84.2)	110 (68.3)	

Values are presented as mean±SD, number (%), or median (IQR). CCI, Charlson comorbidity index; CEA, carcinoembryonic antigen; IQR, interquartile range; SABR, stereotactic ablative radiotherapy; SD, standard deviation. [a)]At the time of local treatment.

ing the study period, the dose fraction schedule was used at the physician's discretion, with the most commonly used schemes being 50 Gy in 5 fractions, 48 Gy in 4 fractions, and 45 Gy in 3 fractions. The mean BED for the SABR group was 112±11 Gy.

3. Endpoint

This study aims to compare the baseline characteristics of patients receiving SABR and metastasectomy to determine when each treatment modality is predominantly used and to compare local control outcomes post-treatment. Local recurrence was defined as progressing lesions either adja-

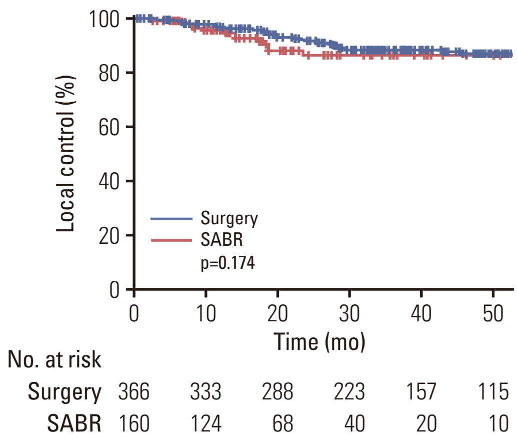

Fig. 2. Kaplan-Meier curve comparing surgery and stereotactic ablative radiotherapy (SABR) for local control.

cent to the staple line or within the irradiated volume, based on longitudinal evaluation of CT images. Local control, the primary study endpoint, was defined as the duration from SABR or surgery administration date to the recurrence near the treatment site, last follow-up, or death. Secondary study endpoints include progression-free survival (PFS) and OS as well as toxicity profiles. PFS was calculated from the date of SABR or surgery administration to disease progression, last follow-up, or death. In contrast, OS was calculated from the date of SABR or surgery administration to last follow-up or death, respectively. Treatment-related toxicities were assessed and graded using Common Terminology Criteria for Adverse Events 5.0. Radiation-related toxicity was collected until the last follow-up after SABR, whereas for surgery, morbidity and mortality were assessed within 1 month post-surgery.

4. Statistical analysis

Recurrence and survival curves were generated using the Kaplan-Meier method. Multivariate analyses for local control, PFS, and OS were conducted using Cox regression analysis. The Charlson Comorbidity Index (CCI) was calculated based on predefined comorbid conditions to assess the overall health status of patients [12]. Statistical significance was defined as $p < 0.05$. All statistical analyses used SPSS ver. 25.0.0 (IBM Corp.).

Results

1. Baseline characteristics at the time of local therapy

The baseline characteristics across the two groups were compared in Table 2. In the surgery group (367 lesions in 334 patients), all patients had wedge resection with R0 resection. Patients who underwent surgery had significantly shorter diagnosis-to-treatment intervals, smaller tumor sizes, more solitary lesions, and less presence of mediastinal lymph nodes. In the SABR group (161 lesions in 70 patients), patients had significantly longer diagnosis-to-treatment intervals, more history of using chemotherapy regimens with bevacizumab or cetuximab, larger tumor sizes, multiple lesions, and a higher incidence of mediastinal lymph node metastasis compared to those who underwent surgery.

Table 3. Univariate and multivariate Cox regression analyses for local control (n=528, per-lesion analysis)

Variable	Univariate analysis		Multivariate analysis[a)]	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Age (as continuous)	0.99 (0.97-1.02)	0.562	-	-
Sex (female vs. male)	1.74 (1.01-2.99)	0.046	-	-
CCI (2 vs. 0-1)	0.83 (0.48-1.43)	0.493	-	-
Diagnosis-to-treatment interval (> 9 vs. ≤ 9 mo)	1.33 (0.76-2.33)	0.317	-	-
Presence of mediastinal lymph node metastasis (yes vs. no)	2.15 (0.66-6.99)	0.201	-	-
No. of pulmonary metastasis (as continuous)	1.12 (0.98-1.29)	0.102	-	-
No. of extrapulmonary metastasis (as continuous)	1.23 (1.13-1.34)	< 0.001	1.21 (1.11-1.32)	< 0.001
CEA level (as continuous)	1.00 (1.00-1.00)	0.527	-	-
Bevacizumab-containing chemotherapy (yes vs. no)	2.05 (1.16-3.64)	0.014	1.83 (1.02-3.28)	0.043
Cetuximab-containing chemotherapy (yes vs. no)	1.35 (0.72 -2.53)	0.347	-	-
Tumor size (as continuous)	1.15 (0.99-1.32)	0.061	-	-
Group (SABR vs. surgery)	0.66 (0.36-1.21)	0.177	-	-

Variables without p-values were included in the initial model but were excluded from the final model. CCI, Charlson comorbidity index; CEA, carcinoembryonic antigen; CI, confidence interval; HR, hazard ratio; SABR, stereotactic ablative radiotherapy. [a)]All variables were initially included in the model, and results were derived using the backward elimination method.

Table 4. Multivariate Cox regression analyses for progression-free survival and overall survival (n=404, per-patient analysis)[a)]

Variable	Progression-free survival		Overall survival	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Age	-	-	1.01 (0.99-1.04)	0.210
Sex (female vs. male)	-	-	-	-
CCI (2 vs. 0-1)	-	-	1.94 (1.19-3.16)	0.008
Diagnosis-to-treatment interval (> 9 vs. ≤ 9 months)	1.28 (0.96-1.69)	0.088	1.00 (0.64-1.55)	0.999
Presence of mediastinal lymph node metastasis (yes vs. no)	2.38 (1.39-4.06)	0.002	8.90 (4.74-16.73)	< 0.001
No. of pulmonary metastasis (as continuous)	1.11 (1.01-1.22)	0.034	1.05 (0.95-1.18)	0.335
No. of extrapulmonary metastasis (as continuous)	1.21 (1.12-1.31)	< 0.001	1.16 (1.04-1.30)	0.007
CEA level (as continuous)	-	-	1.00 (1.00-1.00)	0.400
Bevacizumab-containing chemotherapy (yes vs. no)	1.18 (0.92-1.53)	0.200	-	-
Cetuximab-containing chemotherapy (yes vs. no)	1.61 (1.19-2.19)	0.002	1.63 (1.04-2.55)	0.034
Group (surgery vs. SABR)	0.69 (0.48-0.98)	0.037	0.39 (0.24-0.63)	< 0.001

Variables without p-values were included in the initial model but were excluded from the final model. CCI, Charlson comorbidity index; CEA, carcinoembryonic antigen; CI, confidence interval; HR, hazard ratio; SABR, stereotactic ablative radiotherapy. [a)]All variables were initially included in the model, and results were derived using the backward elimination method.

2. Local control

The median follow-up time was 31.7 months (interquartile range [IQR], 15.3 to 49.7 months). The median follow-up period for SABR group was 23.7 months (IQR, 13.2 to 36.9 months), while the surgery group was 40.8 month (IQR, 27.7 to 59.5 months) ($p < 0.001$). Patients who underwent surgery had 1- and 3-year local control rates of 97.1% and 88.6%, respectively, which were not significantly different from patients treated with SABR, who had 1- and 3-year local control rates of 95.7% and 86.7%, respectively (p=0.174) (Fig. 2). These differences between two groups remained non-significant in multivariate analyses (Table 3). Additionally, the presence of extrapulmonary metastases and patients with *KRAS* or *NRAS* mutation who received bevacizumab-containing chemotherapy also had poorer local control outcomes.

The management of cases of local failure is shown in S1 Table. Treatment of local failure differed between groups. In the surgery group, recurrence was more often confined to the lungs, leading to repeated surgery alongside systemic therapy, with 36.8% of patients undergoing re-operation for local failure. Conversely, in the SABR group, disease progression frequently involved extrapulmonary sites, and most patients (60.0%) received systemic therapy alone without additional local treatment in cases of local failure.

Treatments for mediastinal lymph node metastases were also analyzed (S2 Table). In the surgery group, 12 out of 14 patients underwent surgical resection of the mediastinal lymph nodes. In contrast, in the SABR group, most patients showed a response to systemic therapy, and mediastinal lymph nodes were not typically treated with radiotherapy (RT). Only three out of 23 patients in the SABR group received RT targeting the mediastinal lymph nodes.

3. Systemic treatment

The analysis on systemic treatment was also conducted (S3 Table). We analyzed at which cycle of systemic treatment the local treatment was administered and identified the specific regimens that were used. When comparing the two groups, surgery and SABR, local treatment was most frequently administered during the 2nd cycle of chemotherapy in both groups. The next most common timing for local treatment was during the 1st cycle of chemotherapy. When analyzing the systemic treatment regimens applied, the most commonly used regimen in the surgery group was FOLFOX (folinic acid, fluorouracil, and oxaliplatin; n=86, 25.7%), followed by FOLFIRI (folinic acid, fluorouracil, and irinotecan; n=58, 17.4%) and A-FOLFOX (Avastin-FOLFOX; n=57, 17.1%), respectively. In the SABR group, xeloda (n=21, 30.0%) was the most frequently used regimen, followed by A-FOLFIRI (Avastin-FOLFIRI; n=12, 17.1%). When examining whether systemic treatment was administered alongside local therapy, the majority of patients in the surgery group received systemic treatment (n=256, 76.6%), whereas in the SABR group, more than half of the patients did not undergo systemic treatment (n=40, 57.1%). Additionally, approximately half of the patients (n=157, 47.0%) in the surgery group changed their regimen after local treatment due to disease progression, whereas in the SABR group, 80% of the patients did not change their regimen. Repeated local treatment was performed in cases of progressive disease in more than half of the patients in both groups.

4. Toxicity

Among 334 patients who underwent surgery, 27 patients (8.1%) experienced postoperative complications that required a hospital stay of more than 10 days. However, all patients recovered well, and there were no mortality cases. Additionally, among 70 patients who received SABR, three patients (4.2%) developed symptomatic radiation pneumonitis greater than grade 2. Among these, one patient experienced grade 3 and another grade 4 toxicity (n=2, 2.8%). The patient with grade 4 pneumonitis had received lung SABR for seven lesions. No other grade 3 RT-related toxicities were identified.

5. PFS and OS

The 1-year PFS was 71.1% for the surgery group, 40.8% for the SABR group. The 3-year OS was 45.3% for the surgery group, 27.9% for the SABR group. Prognostic factors for PFS and OS are listed in Table 4. The presence of mediastinal lymph node metastases, an increased number of pulmonary and extrapulmonary metastases, cetuximab-containing chemotherapy and treatment group were independent prognostic factors for PFS. For OS, the independent prognostic factors were CCI, the presence of mediastinal lymph node metastases, and an increased number of extrapulmonary metastases, cetuximab-containing chemotherapy and treatment group.

6. Local therapy for subsequent pulmonary metastases

Among patients who developed new lesions in different locations after the initial local therapy for pulmonary metastases, 36.7% underwent another session of local treatments (surgery, SABR) for the subsequent lesions. Specifically, after surgery, 37.1% of patients required another round of local therapy for pulmonary metastases, with 12.6% undergoing more than two sessions and 2.1% undergoing more than three sessions. Similarly, following SABR, 31.4% of patients received another round of local therapy, with 12.9% having more than two sessions and 7.1% undergoing more than three sessions.

Discussion

In addressing the role of local therapies for pulmonary metastatic disease, one of the highly relevant questions is identifying the most suitable local modality for treating these patients [13]. In this single, large institutional, retrospective comparative study involving 404 patients with 528 pulmonary metastases, we evaluated the treatment outcomes of surgery and SABR as local therapies. Our study demonstrated that SABR was able to achieve excellent local control comparable to surgery, with both groups showing well-tolerated treatments, and low morbidity rates without mortality. A unique aspect of our study is the differentiation based on treatment intent in RT, specifically whether an ablative dose was administered, akin to the distinction between R0 and R1/2 resection in surgery. In cases with multiple lesions or when the treatment intent was to extend the efficacy of systemic therapy for the oligoprogression concept [14], dose-reduced, non-ablative doses (typically a BED less than 100 Gy, such as 30 Gy in 5 fractions or 24 Gy in 3 fractions) can be utilized (S4 Table). As expected, high-dose palliative RT exhibited significantly lower local control rates than the surgery and SABR groups (S5 Fig.).

Our findings regarding local control are in line with the evidence that higher SABR doses, typically with a BED ≥ 100 Gy, result in significantly better local control rates for lung metastases compared to lower doses [15,16]. Guckenberger et al. [17] found that the dose-response curve for local control plateaus around a BED of 100 Gy. This aspect has not been generally properly accounted for in comparative studies between surgery and SABR, leading to the biased conclusion that SABR is inferior to surgery in terms of local control [18].

Another important finding of our study is the significant differences in baseline characteristics selecting RT and surgery for local therapy. Surgery was frequently used upfront when lung metastases were first diagnosed, particularly when the metastases were small, solitary, and without other site metastases. This preference for surgery can be explained by its known advantages over SABR, such as providing a definitive pathological assessment, the potential for complete tumor removal, and eliminating the need for extensive radiologic surveillance [19,20]. Meanwhile, RT was often administered after upfront chemotherapy, typically around one year later, and was preferred for larger tumors, multiple lesions, or when patients had mediastinal lymph node metastases or extrapulmonary disease burden, reflecting the higher risk of disease progression after local therapy as shown in decreased PFS and OS compared to surgery. Furthermore, patients might often be exhausted from previous treatments, such as multiple surgeries or prolonged chemotherapy, and are likely to be inclined towards the minimally invasive nature and shorter recovery time of RT compared to surgery.

If a patient is considered a good candidate for local therapy via multidisciplinary discussion, selecting the best local therapy with the maximized therapeutic index is often not straightforward and involves a significant degree of subjective judgment. For SABR, the proximity of critical organs at risk (e.g., trachea, main bronchus, heart, esophagus, stomach) is a primary consideration, as this can compromise dose coverage planning [21]. In terms of toxicity, the respiratory motion is more significant in the lower lobe than in the upper lobe [22], potentially increasing the irradiated volume, and the availability of respiratory control techniques to reduce the irradiated volume (e.g., gating or tracking) can be a key consideration, especially treating multiple lesions. For surgery, several key factors are generally considered to ensure the best possible outcomes, including palpability, localization, extent of resection, general health, and pulmonary function [13]. Although unavailable at our institution, interventional radiology treatments such as microwave ablation and radiofrequency ablation are also known to control lesions effectively, depending on their location and size [23]. In this context, although there is no widely accepted treatment algorithm, the multidisciplinary approach remains paramount for treatment selection, especially with the active involvement of all local therapy stakeholders to compare the risk/benefit ratio of different modalities [24]. Our findings could provide valuable insights into clinical decision-making in these cases.

Our finding that many patients received subsequent local therapy for recurrent pulmonary metastases has important implications. In well-known oligometastases trials, this figure is around 10%-20% [7,25], and it is expected to be higher in cases of mCRC. Since, unlike the liver, the lung lacks regenerative capacity and has limited pulmonary reserve, it is crucial to prioritize preserving pulmonary reserve, considering that these patients may require multiple treatments.

Our study has several inherent limitations due to its retrospective nature. As shown in the baseline characteristics, selection bias exists between the treatment groups. Despite adjusting for several important factors, significant differences by treatment groups in PFS and OS remain. However, the possibility that more favorable tumors were treated with SABR is low; instead, there is a selection bias towards treating more unfavorable tumors with SABR. The difference in follow-up duration between the treatment groups, with a shorter median follow-up for the SABR group, may limit the ability to fully assess long-term outcomes, highlighting the need for extended follow-up in future studies. Considering these points, the finding that SABR provides equally excellent local control and low overall toxicity compared to surgery is unlikely to change. The fact that our institution is a large-volume single center with experienced surgeons and radiation oncologists can also introduce selection bias, and caution is needed when generalizing these results to low- to intermediate-volume centers. Institutional experience has also been recently suggested to influence SABR's local control outcomes [26], similar to the relationship between volume of experience and surgical outcomes [27]. Since systemic therapy was administered heterogeneously and RT timing varied, elucidating potential interactions between systemic therapy and local control/toxicity to identify the pure component of local therapy was not feasible. Local progression was not pathologically confirmed, but additional positron emission tomography–CT results and monitoring through more than two serial follow-ups were used to determine disease progression. Considering SABR is generally less effective for larger tumors, the small number of patients with large tumor sizes in this study, due to the 3-month short-term image follow-up and early referral, must be taken into account, and thus the results should not be extrapolated to lesions with larger tumor sizes. Our study cannot address whether local therapy confers a survival benefit, or which patients are best suited for local therapy.

In conclusion, we found SABR can achieve excellent local control outcomes similar to surgery. Given the practical difficulty of conducting randomized trials comparing these two modalities for lung metastases, our findings provide important clinical implications. Since patients may require multiple treatments, a patient-centered approach is essential, aiming to preserve lung reserve and minimize morbidity risk while achieving local control. Continued multidisciplinary collaboration within all available local therapy modalities is needed to determine the best local modalities for different situations and locations, understanding the pros and cons of each treatment. With successful collaboration, a hybrid approach, which is not uncommon in the management of liver tumors, could also be investigated for multiple lung lesions [28].

Electronic Supplementary Material

Supplementary materials are available at Cancer Research and Treatment website (https://www.e-crt.org).

Ethical Statement

This study was approved by the institutional review board of Severance Hospital (4-2024-0334), and the requirement for informed consent was waived.

Author Contributions

Conceived and designed the analysis: Yang SY, Kim HS, Koom WS, Park BJ, Chang JS.
Collected the data: Lee BM, Kim HE.
Contributed data or analysis tools: Yang YH, Chang JS.
Performed the analysis: Lee BM, Kim HE, Yang SY, Chang JS.
Wrote the paper: Lee BM, Kim HE, Yang SY, Park BJ, Chang JS.
Investigation: Kim HS.
Validation: Choi SH.
Supervision: Koom WS, Park BJ, Chang JS.
Administration and funding acquisition: Park BJ.
Resources: Chang JS.

ORCID iDs
Byung Min Lee : https://orcid.org/0000-0002-5970-9773
Ha Eun Kim : https://orcid.org/0000-0001-9240-2215
Byung Jo Park : https://orcid.org/0000-0001-5217-4764
Jee Suk Chang : https://orcid.org/0000-0001-7685-3382

Conflicts of Interest

Conflict of interest relevant to this article was not reported.

Funding

This study was supported by the National Research Foundation of Korea (NRF) grant funded by the Korean government (MSIT) (No. NRF-2022R1F1A1074344) and a faculty research grant of Yonsei University College of Medicine (6-2020-0087).

Acknowledgments

We would like to thank Dr. Mitchell Liu from BC Cancer - Vancouver, BC, Canada, for his invaluable contribution. His leadership in establishing regular Lung Ablation Rounds at BC Cancer, where surgeons, radiation oncologists, and interventional radiologists convene to discuss the best approaches, significantly influenced the direction and discussions of this study.

References

1. Qiu M, Hu J, Yang D, Cosgrove DP, Xu R. Pattern of distant metastases in colorectal cancer: a SEER based study. Oncotarget. 2015;6:38658-66.
2. Gonzalez M, Poncet A, Combescure C, Robert J, Ris HB, Gervaz P. Risk factors for survival after lung metastasectomy in colorectal cancer patients: a systematic review and meta-analysis. Ann Surg Oncol. 2013;20:572-9.
3. Bartlett EK, Simmons KD, Wachtel H, Roses RE, Fraker DL, Kelz RR, et al. The rise in metastasectomy across cancer types over the past decade. Cancer. 2015;121:747-57.
4. Timmerman R. A story of hypofractionation and the table on the wall. Int J Radiat Oncol Biol Phys. 2022;112:4-21.
5. Lewis SL, Porceddu S, Nakamura N, Palma DA, Lo SS, Hoskin P, et al. Definitive stereotactic body radiotherapy (SBRT) for extracranial oligometastases: an international survey of >1000 radiation oncologists. Am J Clin Oncol. 2017;40:418-22.
6. Treasure T, Farewell V, Macbeth F, Monson K, Williams NR, Brew-Graves C, et al. Pulmonary Metastasectomy versus Continued Active Monitoring in Colorectal Cancer (PulMiCC): a multicentre randomised clinical trial. Trials. 2019;20:718.
7. Harrow S, Palma DA, Olson R, Gaede S, Louie AV, Haasbeek C, et al. Stereotactic Radiation for the Comprehensive Treatment of Oligometastases (SABR-COMET): extended long-term outcomes. Int J Radiat Oncol Biol Phys. 2022;114:611-6.
8. Liu W, Bahig H, Palma DA. Oligometastases: emerging evidence. J Clin Oncol. 2022;40:4250-60.
9. Ruers T, Van Coevorden F, Punt CJ, Pierie JE, Borel-Rinkes I, Ledermann JA, et al. Local treatment of unresectable colorectal liver metastases: results of a randomized phase II trial. J Natl Cancer Inst. 2017;109:djx015.
10. Thomford NR, Woolner LB, Clagett OT. The surgical treatment of metastatic tumors in the lungs. J Thorac Cardiovasc Surg. 1965;49:357-63.
11. Lee BM, Chang JS, Koom WS, Byun HK, Kim HS, Beom SH, et al. Importance of local ablative therapies for lung metastases in patients with colorectal cancer. Ann Surg. 2023;278:e173-8.
12. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40:373-83.
13. Antonoff MB, Sofocleous CT, Callstrom MR, Nguyen QN. The roles of surgery, stereotactic radiation, and ablation for treatment of pulmonary metastases. J Thorac Cardiovasc Surg. 2022;163:495-502.
14. Lee J, Koom WS, Byun HK, Yang G, Kim MS, Park EJ, et al. Metastasis-directed radiotherapy for oligoprogressive or oligopersistent metastatic colorectal cancer. Clin Colorectal Cancer. 2022;21:e78-86.
15. Nicosia L, Franceschini D, Perrone-Congedi F, Casamassima F, Gerardi MA, Rigo M, et al. A multicenter LArge retrospectIve daTabase on the personalization of stereotactic ABlative radiotherapy use in lung metastases from colon-rectal cancer: The LaIT-SABR study. Radiother Oncol. 2022;166:92-9.
16. Gutierrez E, Sanchez I, Diaz O, Valles A, Balderrama R, Fuentes J, et al. Current evidence for stereotactic body radiotherapy in lung metastases. Curr Oncol. 2021;28:2560-78.
17. Guckenberger M, Wulf J, Mueller G, Krieger T, Baier K, Gabor M, et al. Dose-response relationship for image-guided stereotactic body radiotherapy of pulmonary tumors: relevance of 4D dose calculation. Int J Radiat Oncol Biol Phys. 2009;74:47-54.
18. Nelson DB, Tayob N, Nguyen QN, Erasmus J, Mitchell KG, Hofstetter WL, et al. Local failure after stereotactic body radiation therapy or wedge resection for colorectal pulmonary metastases. J Thorac Cardiovasc Surg. 2019;158:1234-41.
19. van Dorp M, Trimbos C, Schreurs WH, Dickhoff C, Heineman DJ, Torensma B, et al. Colorectal pulmonary metastases: pulmonary metastasectomy or stereotactic radiotherapy? Cancers (Basel). 2023;15:5186.
20. Malik NH, Keilty DM, Louie AV. Stereotactic ablative radiotherapy versus metastasectomy for pulmonary metastases: guiding treatment in the oligometastatic era. J Thorac Dis. 2019;11:S1333-5.
21. Van Oirschot M, Bergman A, Verbakel W, Ward L, Gagne I,

Huang V, et al. Determining planning priorities for SABR for oligometastatic disease: a secondary analysis of the SABR-COMET phase II randomized trial. Int J Radiat Oncol Biol Phys. 2022;114:1016-21.
22. Wang Y, Bao Y, Zhang L, Fan W, He H, Sun ZW, et al. Assessment of respiration-induced motion and its impact on treatment outcome for lung cancer. Biomed Res Int. 2013;2013: 872739.
23. Matsui Y, Tomita K, Uka M, Umakoshi N, Kawabata T, Munetomo K, et al. Up-to-date evidence on image-guided thermal ablation for metastatic lung tumors: a review. Jpn J Radiol. 2022;40:1024-34.
24. Choi SH, Yang G, Koom WS, Yang SY, Kim SS, Lim JS, et al. Active involvement of patients, radiation oncologists, and surgeons in a multidisciplinary team approach: guiding local therapy in recurrent, metastatic rectal cancer. Cancer Med. 2023;12:21057-67.
25. Liu W, Das S, Olson RA, Baker S, Dunne EM, Chang JS, et al. Polymetastatic recurrence-free survival in patients with repeat oligometastases on the SABR-5 trial. Int J Radiat Oncol Biol Phys. 2023;117(2 Suppl 1):S59.
26. Rieber J, Abbassi-Senger N, Adebahr S, Andratschke N, Blanck O, Duma M, et al. Influence of institutional experience and technological advances on outcome of stereotactic body radiation therapy for oligometastatic lung disease. Int J Radiat Oncol Biol Phys. 2017;98:511-20.
27. Rottoli M, Spinelli A, Pellino G, Gori A, Calini G, Flacco ME, et al. Effect of centre volume on pathological outcomes and postoperative complications after surgery for colorectal cancer: results of a multicentre national study. Br J Surg. 2024; 111:znad373.
28. Harrison OJ, Sarvananthan S, Tamburrini A, Peebles C, Alzetani A. Image-guided combined ablation and resection in thoracic surgery for the treatment of multiple pulmonary metastases: a preliminary case series. JTCVS Tech. 2021;9:156-62.