

Salvage pulmonary resection after stereotactic body radiotherapy: A feasible and safe option for local failure in selected patients



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ABSTRACT

Objective: For inoperable patients with pulmonary malignancy, stereotactic body radiotherapy is a reasonable therapeutic option. Despite good early tumor control, local failure occurs in up to 10% of patients by 3 years. Because management of local recurrence after stereotactic body radiotherapy is unclear, we evaluated use of surgery as a salvage option.

Methods: A retrospective review was conducted of consecutive patients from a single institution who underwent salvage resection of primary and metastatic pulmonary malignancies previously treated with stereotactic body radiotherapy. In addition, a literature search was conducted to identify previous reports of pulmonary resection for local stereotactic body radiotherapy failures, to allow cumulative analyses with previously published cases.

Results: A total of 21 patients met inclusion criteria. The median time between stereotactic body radiotherapy and salvage surgery was 16.2 months (range, 6.4-71.5). Postoperative complications occurred in 7 patients (18.9%), in whom atrial arrhythmias and prolonged air leaks (>5 days) were most frequent (n = 2 each, 5.4%). There was no local recurrence after salvage surgery. Distant failure occurred in 5 of 21 patients (23.8%) at a median of 36.2 months, and median disease-free survival was 19.2 months. The 30- and 90-day mortality was 4.8% (1 patient). Cumulative analysis included 37 patients from 4 institutions and comprised 26 (78.8%) primary non-small cell lung cancers and 11 (29.7%) lung metastases. Median overall survival after salvage surgery was 46.9 months, and 3-year survival was 71.8%.

Conclusions: After local failure of stereotactic body radiotherapy, salvage resection remains a viable option for operable patients, with acceptable morbidity and survival. As use of stereotactic body radiotherapy continues to expand, further studies to evaluate the optimal management for local failure are needed. (J Thorac Cardiovasc Surg 2017;154:689-99)

For early-stage non-small cell lung cancer (NSCLC), operative resection consisting of lobectomy and mediastinal lymph node dissection has been a long-standing, established standard of care.¹ For patients thought to be

inoperable or with prohibitively high operative risk, novel therapeutic options have been introduced in recent years through advances in radiotherapy.² Stereotactic body radiotherapy (SBRT) is a means of delivering high doses of external beam radiation over a limited number of treatment fractions to an image-defined target, and it has become a

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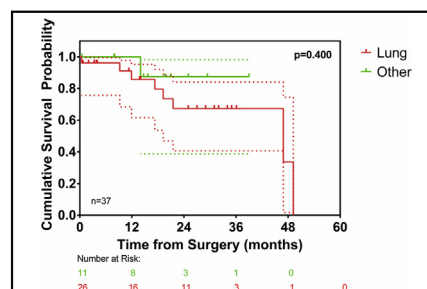
Received for publication May 2, 2016; revisions received Feb 23, 2017; accepted for publication March 25, 2017; available ahead of print May 9, 2017.

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0022-5223/\$36.00

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<http://dx.doi.org/10.1016/j.jtcvs.2017.03.142>



Survival after salvage surgery for failed SBRT.

Central Message

Operative resection after local failure of SBRT in highly select individuals is feasible and safe, and has an overall acceptable morbidity and mortality.

Perspective

This study represents the largest series of pulmonary resection after local SBRT failure reported to date, along with a cumulative review that incorporates all patients who have been previously reported. We demonstrate that resection after local failure of SBRT in highly select individuals is feasible and safe, and has an overall acceptable morbidity and mortality, albeit higher than what is typically observed in nonirradiated patients.

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Scanning this QR code will take you to a supplemental video. To view the AATS 2016 Webcast, see the URL next to the webcast thumbnail.



Abbreviations and Acronyms

CT	= computed tomography
DLCO	= diffusing capacity of the lung for carbon monoxide
FEV1	= forced expiratory volume in 1 second
FDG	= fluorodeoxyglucose
GT	= General Thoracic
MDACC	= MD Anderson Cancer Center
NSCLC	= non-small cell lung cancer
PET	= positron emission tomography
SBRT	= stereotactic body radiotherapy
STS	= Society of Thoracic Surgeons

viable option for the management of patients with early NSCLC unable to tolerate surgical resection.²⁻⁴ Several single-institution studies have demonstrated SBRT to be an efficacious and well-tolerated treatment strategy in medically inoperable patients with early-stage lung cancer.^{3,5,6} The Radiation Therapy Oncology Group 0236 trial, subsequently published in 2010, prospectively evaluated SBRT among patients at multiple North American centers, revealing high rates of local tumor control with acceptable treatment-related morbidity.⁷ Other investigators have further corroborated these findings, with reproducibly acceptable rates of intermediate-term local control and minimal toxicities.⁸⁻¹⁰

Given the success of using SBRT for stage I NSCLC in medically inoperable patients, increasing interest has arisen regarding the potential application of this modality for healthier, potentially operable patients.¹¹⁻¹³ Although some early studies have demonstrated encouraging evidence, they have been inconclusive, and despite the initiation of several randomized trials, accrual has been a challenge.¹¹ In addition, the use of SBRT has been extended in a number of centers to include pulmonary metastases, in addition to primary lung cancer. Important issues warranting investigation will include determination of the ideal means of following patients radiographically after SBRT and establishing protocols for intervention on local failure.

The outcomes for salvage lung resection after SBRT are not well established. Previous experiences have been described in 4 small case series, with a suggestion of reasonable perioperative morbidity and local control, among patients with NSCLC and those undergoing treatment for pulmonary metastatic disease.¹⁴⁻¹⁷

In this study, we aimed to evaluate our experience with operative lung resection in patients in whom SBRT has failed. Further, we review the combined outcomes in patients from our center along with those previously reported in the published literature.

MATERIALS AND METHODS**MD Anderson Cancer Center Institutional Analysis**

After obtaining Institutional Review Board approval (PA-0169), we used our departmental surgical database to identify all patients who underwent salvage pulmonary resection after prior radiation between January 1, 2009, and September 30, 2015. Patient medical records were reviewed, and only patients in whom the lesion in question was previously treated with SBRT and then underwent salvage resection for local recurrence were selected. Patients were excluded if the prior radiation was inconsistent with SBRT techniques or if the SBRT was delivered to a lesion other than that which was subsequently resected. All patients underwent surgery at MD Anderson Cancer Center (MDACC); however, not all patients received SBRT at our institution. Among 716 patients who underwent pulmonary resection after previous radiotherapy, only 21 were identified who met inclusion criteria, and these patients comprised the MDACC study cohort.

Detailed patient data were retrospectively collected from our departmentally maintained, prospectively entered database and supplemented with additional chart review. Variables collected included information pertaining to demographics, histology, staging, radiation dosing and fractions, patient comorbidities and operability, extent of resection, recurrence, and vital status.

Aggregate Analysis

In addition, a MEDLINE search was performed to identify all previous reports of surgical resection after local failure after initial treatment with SBRT. Searches were performed in September 2015, limited to English language literature, and using the following search terms: “salvage surgery,” “salvage resection,” along with “lung” and “pulmonary,” as well as “SBRT,” “SABR,” and “stereotactic radiation.” This resulted in 56 articles, which were reviewed by 2 of the authors (MBA and DCR) to specifically identify publications regarding lung resection after local recurrence after SBRT. Four studies were identified, totaling 18 patients; however, because Taira and colleagues¹⁷ included resection of specimens lacking any residual disease, we chose to use only the other 3 reports for cumulative analyses.¹⁴⁻¹⁷ From these previous publications, data were extracted for each patient, including age, sex, histology, staging, operability, radiation dosing and fractions, extent of resection, any other available operative details, and disease status/vital status at last follow-up. The data from the patients in these publications were combined with those of the MDACC cohort, thus constituting the final aggregate cumulative group.

For analyses of both the MDACC and the cumulative groups, continuous variables are reported as median and range, and categorical variables are presented as N and %. Student paired *t* tests were used to compare pre-SBRT and presalvage surgery pulmonary function test results, with a 2-sided *P* value of .05 considered significant. Kaplan-Meier analyses were performed to evaluate survival from the time of surgery and survival from completion of SBRT. All statistical analyses were performed using IBM SPSS statistics version 23.0 (IBM Corporation, Armonk, NY).

RESULTS**Patients**

At MDACC, 21 individuals met inclusion criteria and comprise the MDACC group, consisting of 15 patients (71.4%) with primary NSCLC and 6 patients (28.6%) with pulmonary metastatic disease (Table 1). The cumulative group included 37 patients at 4 institutions, including 26 (70.2%) with NSCLC (17 [65.4%] squamous cell, 7 [26.9%] adenocarcinoma, and 2 [7.7%] NSCLC not otherwise specified). Eleven patients (29.7%) underwent pulmonary resection for recurrent metastases, including 7

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