Percutaneous Cryoablation of Metastatic Lesions from Non–Small-Cell Lung Carcinoma: Initial Survival, Local Control, and Cost Observations

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ABSTRACT

Purpose: To assess feasibility, complications, local tumor recurrences, overall survival (OS), and estimates of cost effectiveness for multisite cryoablation (MCA) of oligometastatic non–small-cell lung cancer (NSCLC).

Materials and Methods: A total of 49 computed tomography- and/or ultrasound-guided percutaneous MCA procedures were performed on 60 tumors in 31 patients (19 women and 12 men) with oligometastatic NSCLC. Average patient age was 65 years. Tumor location was grouped according to common metastatic sites. Median OS was determined by Kaplan–Meier method and defined life-years gained (LYGs). Estimates of MCA costs per LYG were compared with established values for systemic therapies.

Results: Total numbers of tumors and cryoablation procedures for each anatomic site were as follows: lung, 20 and 18; liver, nine and seven; superficial, 12 and 11; adrenal, seven and seven; paraaortic/isolated, two and two; and bone, 10 and seven. A mean of 1.6 procedures per patient were performed, with a median clinical follow-up of 11 months. Major complication and local recurrence rates were 8% (four of 49) and 8% (five of 60), respectively. Median OS for MCA was 1.33 years, with an estimated 1-year survival rate of approximately 53%. MCA appeared cost-effective even when added to the cost of best supportive care or systemic regimens, with an adjunctive cost-effectiveness ratio of $49,008–$87,074.

Conclusions: MCA was associated with very low morbidity and local tumor recurrence rates for all anatomic sites, and possibly increased OS. Even as an adjunct to systemic therapies, MCA appeared cost-effective for palliation of oligometastatic NSCLC.

ABBREVIATIONS

ACER = adjunctive cost-effectiveness ratio, BSC = best supportive care, LYG = life-year gained, MCA = multisite cryoablation, mNSCLC = metastatic non–small-cell lung cancer, NSCLC = non–small-cell lung cancer, OS = overall survival, PET = positron emission tomography, QALY = quality-adjusted life-year, RF = radiofrequency

Lung cancer is the leading cause of cancer-related deaths, with an estimated 222,520 new diagnoses and 157,300 deaths in the United States in 2010. Non–small-cell lung cancer (NSCLC) is the most prevalent form, accounting for approximately 85% of all lung cancers (1). Approximately 7% of patients with NSCLC, or 15,576 per year in the United States, will initially present with limited or oligometastatic disease (2,3). Survival for patients with NSCLC varies considerably depending on stage, with a 5-year survival rate of 15.8% observed in all cases and a 5-year survival rate of 3.5% observed in patients with metastatic disease (4).

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Table 1. Patient, Procedure, and Tumor Characteristics

			Soft Tissue					
Location	Lung	Liver	Superficial	Adrenal	Paraaortic/Isolated	Bone	Subtotal*	Total*
No. of patients	13	6	4	7	2	6	15	31
No. of procedures	18	7	11	7	2	7	25	49
No. of tumors	20	9	12	7	2	10	31	60
Average tumor diameter (cm^3)	2.6	2.7	2.8	4.3	2.2	4.3	3.6	3.1
Average ablation diameter (cm^3)	4.4	5.2	5.1	5.9	4.5	6.5	5.7	5.2

Note.—Lung tumor locations consisted of metastatic lesions in lung parenchyma and/or chest wall but did not include mediastinal or hilar adenopathy. Superficial tumor locations consisted of predominantly subcutaneous, muscular, and/or lymph node metastases within the extremities or torso wall. Tumors in bone locations were limited metastatic deposits in non–weight-bearing locations with the epicenter in osseous structures.

* Totals do not equal the sum because soft tissue is broken down into four categories and there is overlap in the total. Repeat treatment of a single tumor, as well as a single procedure involving multiple locations, also causes totals to overlap.

The primary treatment for patients with advanced NSCLC is platinum-based chemotherapy but is mainly for palliation because survival generally only increased to 6 months, versus 4.5 months for best supportive care (BSC) (5,6). Targeted treatments such as bevacizumab further extended survival to 14 months, but this agent is safe in only nonsquamous cell carcinoma because of bleeding risks (7–9). Radiation therapy is effective in palliation of NSCLC symptoms but offers limited survival benefits of less than 10% at 2 years for high- and low-dose treatment (10). Regardless of the specific treatment, nearly all NSCLC patients who receive systemic therapy will eventually experience a disease relapse (5,11).

Minimally invasive ablation techniques such as radiofrequency (RF) ablation and cryoablation offer unique benefits in the management of symptomatic and/or isolated metastases (12–14). RF ablation may be more limited in its ability to treat metastases in diverse soft tissue locations, such as near the skin or in close proximity to crucial structures (15). The visible treatment zone of cryoablation, lower pain, and better healing allowed us to apply our established cryoablation techniques (16–21) to many anatomic sites for local control of limited metastatic (oligometastatic) NSCLC.

The purpose of this study was to assess the potential role of multisite cryoablation (MCA) of oligometastatic NSCLC by evaluating complications, local recurrences, survival, and projected procedure costs in relation to systemic treatments. Estimates of MCA cost-effectiveness were compared to BSC and emerging chemotherapy/targeted therapy regimens (22–24) to place an economic perspective on our outcomes for this select group of patients.

MATERIALS AND METHODS

Patients

Consecutive patients with limited (oligometastatic) NSCLC read and signed an authorization form issued under the Health and Insurance Portability and Accountability Act of 1996. All patients also signed a separate consent form detailing the procedure, as well as an investigational review board–approved consent form for prospective collection of procedure, imaging, and clinical parameters. Average patient age was 65 years (range, 45–90 y) at the time of the first procedure. The six procedural locations included lung, liver, and four soft tissue sites: adrenal, paraaortic/isolated, superficial, and bone (**Table 1**).

Inclusion criteria for cryoablation consisted of a localized mass smaller than 7 cm that was biopsy-proven, deemed suspicious based on a computed tomography (CT) scan showing an enhancing or growing mass, or found positive on a positron emission tomography (PET) scan. Patients should not have more than five cancerous foci in an organ site to avoid compromising safety in patients with advanced disease to allow MCA to treat all metastases present at the time of the first procedure over the course of one or multiple procedures. These patients were generally referred by oncologists for local control of oligometastatic NSCLC. Tumors in different locations were treated in single or multiple staged cryoablation procedures according to projected feasibility and/or safety. MCA also referred to additional foci developing over time that were targeted for local control in subsequent procedures. All cases were reviewed and performed by a single radiologist with 20 years of interventional and cross-sectional imaging experience (P.J.L.).

The patients included in this study were retrospectively confirmed as having metastatic NSCLC (mNSCLC) through thorough review of their patient charts, pathology reports, imaging findings, and correlation with PET positive lesions. Patients with pulmonary lesions were deemed positive for metastatic disease only if other discrete metastases were already present, as a metastatic focus is then much more likely than a second primary tumor. Patients who were proven to have locally recurrent tumors after chemotherapy/radiation therapy, surgical resection, or previous ablation without biopsy-proven metastatic lung cancer were excluded from this study. Also, patients with biopsy-proven lesions suspicious for a second primary tumor or a meta-

Table 2. Patients Receiving Systemic Regimens before or after MCA

Timing	Erlotinib	Cisplatin/ Vinorelbine	Cisplatin/ Gemcitabine	Paclitaxel/ Carboplatin	Bevacizumab/ Paclitaxel/ Carboplatin	Other	Total
Before MCA	3 (10)	0	1 (3)	6 (19)	2 (6)	18 (58)	26 (84)*
After MCA	2 (6)	0	0	1 (3)	0	8 (26)	11 (35)
Total	5 (16)	0	1 (3)	7 (23)	2 (6)	26 (84)	26 (84)†

Note.—Values in parentheses are percentages. MCA = multisite cryoablation.
* Multiple patients received more than one systemic regimen, which results in overlapping data. The actual number of patients receiving chemotherapy/targeted therapy before MCA was 26.
† Some patients received chemotherapy/targeted therapy before and after MCA, resulting in overlapping data. The actual number of patients receiving systemic regimens at some point was 26.

static lesion from an extrathoracic primary tumor were excluded from this study. Patient charts were reviewed by a pulmonary oncologist with more than 20 years of experience (S.G.). Patients who received BSC or any chemotherapy or targeted therapy regimen before or after MCA were also noted. For comparison in our cost evaluations, these regimens included erlotinib (Tarceva; Genentech/OSI, Melville, New York), cisplatin with vinorelbine, cisplatin with gemcitabine, paclitaxel with carboplatin, and bevacizumab with paclitaxel and carboplatin. **Table 2** displays the administration of these systemic regimens in our patient group.

Cryoablation Procedure

The primary technical goal for cryoablation procedures was to achieve sufficient probe distribution (eg, approximately one cryoprobe for each centimeter of tumor diameter) to reach cytotoxic temperatures less than −20°C covering all tumor margins. Probe type (ie, 1.7- or 2.4-mm outer diameter) and number were recorded for each ablation site. Cryoablation planning techniques/procedural details and associated hydrodissection protection measures for renal, pulmonary, soft tissue, and breast tumors have been previously described (16–21).

Imaging and Follow-up

Real-time ultrasound (LOGIQ 700; GE Medical Systems, Milwaukee, Wisconsin) was used to place and monitor cryoprobes during procedures solely in superficial locations, which consisted of predominantly subcutaneous, muscular, and/or lymph node metastases within the extremities or torso wall. CT was used as the primary imaging modality for planning, procedure guidance, and treatment follow-up in the remaining procedural sites. Magnetic resonance (MR) imaging was used as needed for improved tissue/tumor discrimination or iodine allergies. Tumors and ablation zones were measured in three dimensions and noted on axial images in their greatest transverse and anteroposterior extent, with sagittal and/or coronal reconstructions used to obtain craniocaudal measurements. In follow-up, enhanced CT or MR images were obtained at 1, 3, 6, 12, 18, and 24 months and yearly thereafter as available.

Complications

All treatment-related complications were categorized in accordance with the Common Terminology Criteria for Adverse Events, version 3.0, of the National Cancer Institute, similar to published cryoablation series (17–19). Complications were not linked to cost estimates. A formal decision analysis model was not yet considered appropriate for initial cost-effectiveness estimates.

Recurrences

The therapeutic goal of cryoablation is to achieve complete ablation of a tumor focus with minimal damage to surrounding soft tissues. However, tumor recurrence may occur at the site of cryoablation. Local recurrences were separated into procedural and satellite etiology and do not address additional metastatic disease because disease were stage 4 and the patients were treated for palliation. A procedure-related recurrence was defined as any recurrence within the ablation zone resulting from an inadequate, sublethal isotherm likely along the tumor rim (positive margins). Satellite lesions were located less than 1 cm beyond the ablation zone, likely resulting from adjacent microscopic foci of the tumor.

Survival

Overall survival (OS) was analyzed by using the Kaplan–Meier estimator in the Lifetest procedure in SAS software (version 9.2; SAS Institute, Cary, North Carolina). Progression-free survival was deemed not appropriate for evaluation of a local treatment in patients treated only for palliation of symptoms. Therefore, additional sites of disease progression were not assessed after ablation. OS was measured from the time of the first MCA procedure until death or until the most recent follow-up for vital status determination. Because of modest sample sizes (or numbers of events), OS statistics (eg, median, 1-y rate) were estimated more conservatively by using linear interpolation between successive event times on the Kaplan–Meier curve (25). All point estimates of OS statistics were accompanied by a 95% CI. OS for MCA was compared to OS for BSC and five established mNSCLC regimens: erlotinib (Tarceva), cisplatin with vinorelbine, cisplatin with gemcitabine, paclitaxel

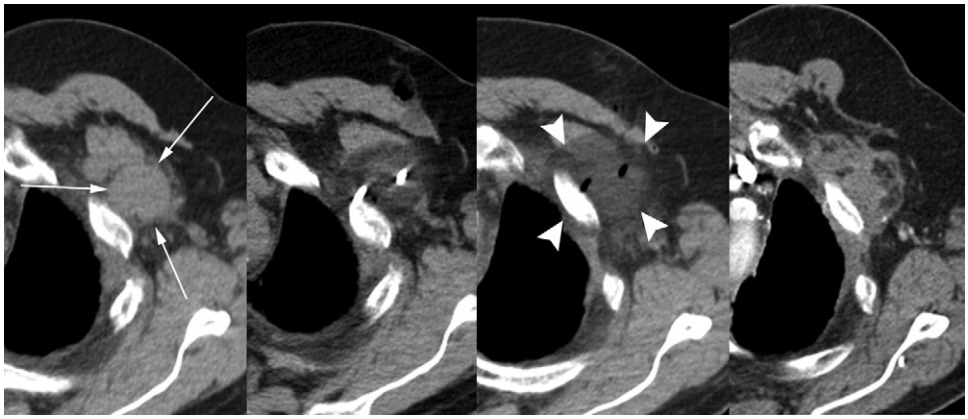

Figure 1. Images from a 68-year-old man with metastatic adenocarcinoma who received localized radiation treatment to the chest and had discontinued erlotinib because of diffuse skin eruptions. He presented with a left chest wall metastatic lesion abutting the second rib near the site of a previous thoracotomy for a left lung mass 1 year earlier. Images (from left to right) show the preoperative, intraprocedural, immediate postablation, and 2-year follow-up enhanced axial CT appearance of the mass. Initial measurements were 5.1 × 3.2 × 4.0 cm (image 1, arrows), and the mass resorbed into a diffusely hypovascular mass measuring 3.8 × 2.2 × 2.0 cm approximately 22 months later. A well demarcated hypodense ablation zone (image 3, arrowheads) is shown on immediate postablation axial CT.

with carboplatin, and paclitaxel with carboplatin and bevacizumab (22–24).

Cost

We explored inflated cost estimates for MCA to gain insight whether the palliative use of MCA had reasonable potential for future more detailed cost-effectiveness analyses. Our cost estimates also contain billing charges, rather than estimates of direct and/or indirect costs (26). These cost estimates served as a potential economic counterbalance to any survival benefit noted for MCA, especially as ablation may be perceived as only adding costs to a palliative treatment in an advanced disease state.

A total cost of $11,000 per cryoablation procedure represents a high-end estimate from mean professional fees ($2,000), disposable equipment fees ($4,000 for three cryoprobes), and hospital fees ($5,000). Mean cost of more frequent follow-up imaging examinations of $42,000 encompassed six follow-up CT imaging sessions at $7,000 each (eg, at 1, 3, 6, 12, 18, and 24 mo and yearly thereafter). Each CT session reflected our institution's 2010 Medicare technical component guidelines of $2,171, $2,396, and $1,390 for chest, abdominal, and pelvic CT, respectively, and professional fees of approximately $350 per scan. No significant cost difference was assumed for MR imaging based on our 2010 Medicare guideline of $2,171 for each MR examination per anatomic site. The mean number of procedures per patient was used to determine the cost per patient. The overlapping schedule in follow-up imaging after a second ablation did not justify counting follow-up imaging charges more than once.

Additionally, patients in this study may have had chemotherapy/targeted treatments at some point. Costs of MCA were therefore also considered in an adjunctive role and added to each therapy comparison, then divided by the overall life-years gained (LYGs) for MCA in this study. We termed this approach an adjunctive cost-effectiveness ratio (ACER) to more accurately estimate scenarios encountered by our patients. ACERs lower than $100,000 per LYG were considered cost-effective (27).

RESULTS

Patients, Procedure, and Follow-up

A total of 31 patients underwent 49 procedures on 60 tumors (**Table 1**). The mean number of procedures per patient was 1.6. The cryoablation zone was well defined by CT as a hypodense ice ball (**Figs 1, 2**) with an average ablation diameter of 5.2 cm, generated by mean of 3.4 probes per patient for a mean tumor diameter of 3.1 cm. Of our patients, 84% (26 of 31) and 35% (11 of 31) received some form of chemotherapy/targeted therapy before or after MCA, respectively, with a total of 84% (n = 26) receiving a systemic regimen at some point. **Table 2** details the administration of these regimens in our patient group.

Complications

Overall, cryoablation procedures on this patient cohort resulted in an 8% incidence of complications of grade 3 or worse (four of 49 procedures). A detailed breakdown of complication grade and location is shown in **Table 3**. One patient undergoing an ablation of a metastasis on the chest wall (**Fig 3**) experienced a grade 4 pericardial tamponade. A pericardiocentesis was performed to remove 300 mL of clear fluid from the pericardium, after which blood pressure increased from 130 to 180 mm Hg and pulse decreased from 130 to 110 beats/min. A complication in another patient was classified as grade 5 because his death occurred

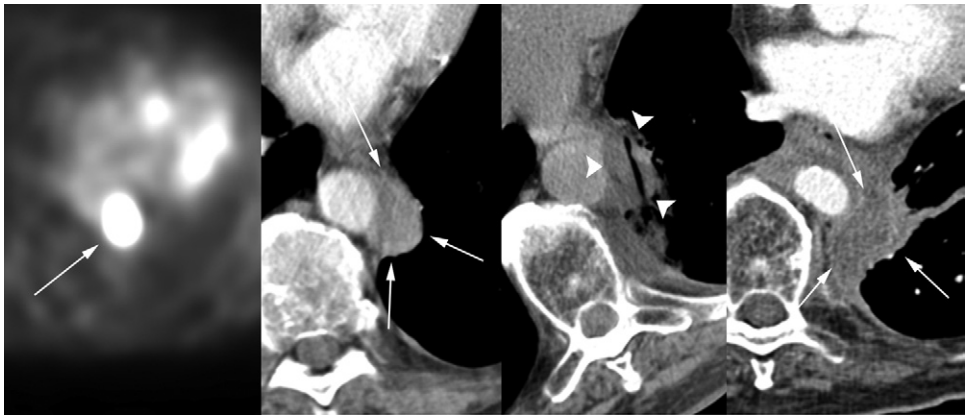

Figure 2. The 68-year-old patient shown in **Figure 1** was found to have a [^{18}F]fludeoxyglucose PET-positive left paraaortic node (image 1, arrow) 4 months after the ablation procedure shown in **Figure 1**. This enhancing lesion measuring 1.8 × 3.5 × 4.2 cm (image 2, arrows) was treated with cryoablation (image 3, arrowheads), resulting in a resorbed hypodense nonenhancing soft-tissue site on follow-up axial CT (image 4, arrows). As demonstrated in the third image, well demarcated hypodense margins of the ice ball allow safe ablation adjacent to crucial structures such as the aorta.

Table 3. Complication Rates per Procedure by Anatomic Location

Location	No. of Procedures	Grade				Grade > 3 Complications
		1/2	3	4	5	
Lung	18	6	1	—	1	2
Liver	7	2	—	—	—	—
Soft tissue						
Superficial	11	1	—	—	—	—
Adrenal	7	1	—	—	—	—
Paraaortic/isolated	2	—	—	—	—	—
Bone	7	—	1	1	—	2
Subtotal	25*	2	—	—	—	—
Total	49†	10 (20)	2 (4)	1 (2)	1 (2)	4 (8)

Note.—Values in parentheses are percentages.
* Two patients had a procedure involving two soft tissue locations. The actual procedure count is 25.
† One patient had one procedure in soft tissue and lung locations. The actual procedure count is 49.

within the 1-month window after the procedure; however, it was deemed unrelated to treatment.

Recurrences

The mean follow-up time for all patients was 11 months (range, 0–60 mo), and **Table 4** shows the local recurrences by anatomic region. Procedures on 60 tumors resulted in a 2% procedural recurrence rate (one of 60) and a 7% satellite recurrence rate (four of 60), for an overall local recurrence rate of 8%. Average time to recurrence was 4 months.

Survival

The calculated OS is shown in **Figure 3**. Of the original 31 patients, 27 have died as of the time of manuscript preparation. The mean observed OS was 15.9 months, or 1.33 years. Projected 1-year survival rate was approximately 53% for these patients. **Figure 4** displays the estimated OS of patients who received only BSC following their first MCA procedure (median survival, 16.5 mo) versus patients who received systemic therapy before and after MCA (median survival, 12 mo).

Cost

In all cases, "upper-bound" cost estimates produced a total cost of each cryoablation procedure and frequent imaging follow-up of $53,000 ($11,000 per procedure plus $42,000 total for imaging follow-up). Multiple metastatic lesions were treated in an average of 1.6 procedures per patient, making the estimated upper cost per patient of $59,600 (ie, $11,000 * 1.6 + $42,000).

Table 5 demonstrates our ACER evaluations for MCA based on comparisons with established values for five mNSCLC therapies: BSC, erlotinib, cisplatin with vinorelbine, cisplatin with gemcitabine, paclitaxel with carboplatin, and paclitaxel with carboplatin and bevacizumab (22–24). Our MCA estimate of cost per total LYG of $44,812 (ie, $59,600 divided by 1.33) appears encouraging for future detailed analysis, especially as the

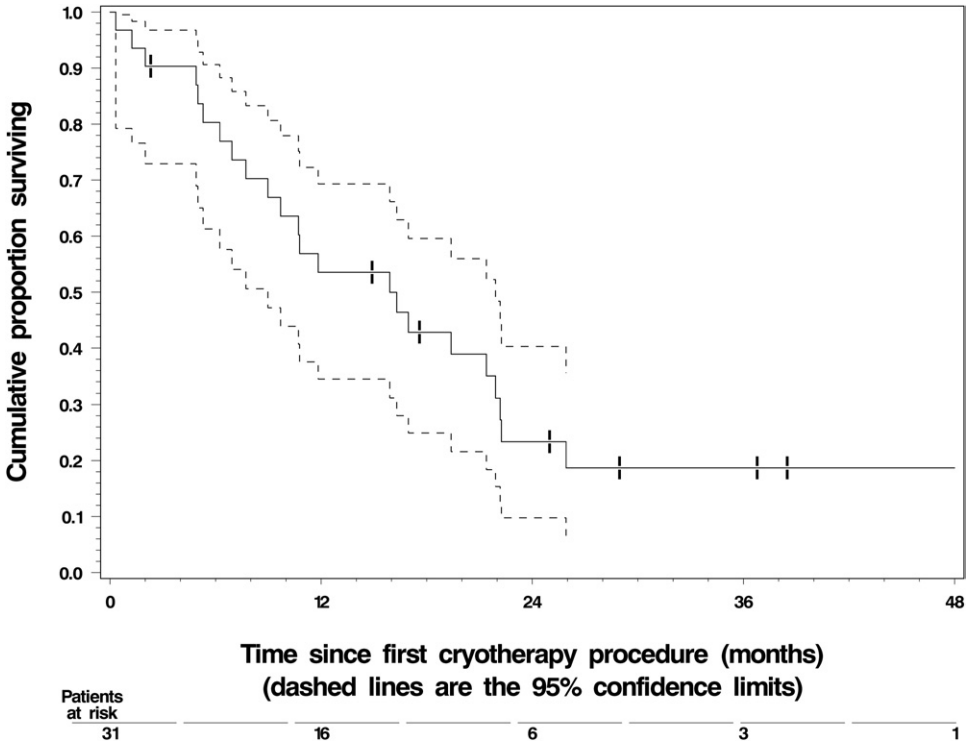

Figure 3. Kaplan–Meier estimate of OS in the 31 study-eligible patients. The dashed lines represent the 95% CI of each successive estimate of the survival rate. The median OS was 15.9 months (1.33 y; 95% CI, 8.9–21.9 mo). The 1-year OS rate was 53% (95% CI, 35%–71%).

Table 4. Local Tumor Recurrence by Anatomic Location

Location	No. of Tumors	Average Tumor Diameter (cm)	Procedural (Type 1)	Satellite (Type 2)	Total Local Recurrences	Mean Time to Recurrence (mo)
Lung	20	2.6	1	1	2	4
Liver	9	2.7	—	2	2	—
Soft tissue						
Superficial	12	2.8	—	1	1	10
Adrenal	7	4.3	—	—	—	—
Paraaortic/isolated	2	2.2	—	—	—	—
Bone	10	4.3	—	—	—	2
Subtotal	31	3.6	—	—	—	—
Total	60	3.1	1 (1.7)	4 (6.7)	5 (8.3)	—

Note.—Of the five total recurrences, three satellite recurrences (one lung, two liver) were noted to have occurred within the presence of major vasculature. Although it is possible these recurrences may be attributed to adjacent microscopic satellite foci, it is also possible the vessels created a heat-sink effect resulting in incomplete ablation of all tumor margins. Values in parentheses are percentages.

ACER for MCA was cost-effective versus all chemotherapy/targeted therapy protocols, with the average being $60,610 per LYG.

DISCUSSION

This study suggests feasibility, safety, and potential cost-effectiveness of MCA as an adjunct to the palliative care of patients with oligometastatic NSCLC. We first summarize our findings and then address specific implications. The estimated 1-year survival rate observed in our patient population of approximately 53% and a median OS of 15.9 months suggests extended survival versus known systemic options; this is also an increase compared with the observed survival of patients receiving only BSC, which typically cannot provide median survival beyond 6 months. Low rates of local recurrences and complications in our patient group suggest feasibility and safety, and did not appear dependent on tumor location. Overall, 84% of our patients received systemic treatment at some point, with multiple

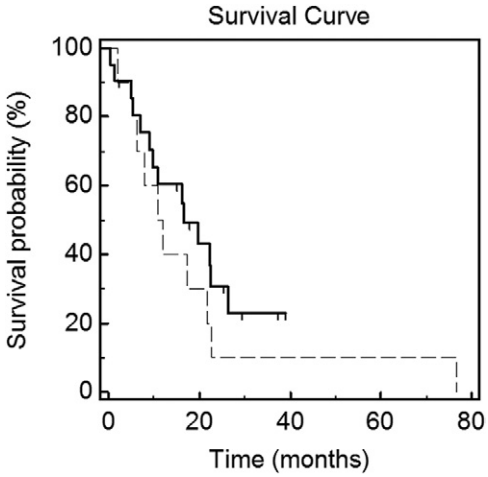

Figure 4. Kaplan–Meier estimate of OS for patients who received chemotherapy/targeted therapy regimens before and after MCA (dashed line) versus patients who received no systemic therapy following MCA (solid line). The median OS was 12 months for patients who were administered systemic therapy before/after MCA, and the median OS was 16.5 months for patients who received only BSC after MCA.

regimens failing in many cases. Of our patients, 65% received no chemotherapy/targeted therapy after MCA, indicating MCA alone is capable of achieving at least local control of oligometastatic NSCLC.

Although a relatively low percentage of cases present with oligometastatic NSCLC, these patients still represent nearly 20,000 cases, not including cases of local failure after chemotherapy (28). The ability to provide local control for persistent disease foci is important when addressing treatment options, particularly when metastases can present in multiple locations. A unique aspect of cryoablation versus heat-based (ie, RF or microwave) ablations is its flexibility for pulmonary and soft-tissue locations, which are commonly observed in mNSCLC; for instance, hepatic, adrenal, bone, and abdominal lymph node metastases are seen in as many as 29%–40% of patients with mNSCLC (29), and more than 58% of our patients (18 of 31), or 52% of tumors (31 of 60), were treated for soft-tissue metastases. For centrally located pulmonary metastases, cryoprobes can be placed closely to mediastinal and hilar vessels under CT guidance to negate the thermal exchange occurring between vasculature and the ablation zone without fear of damaging vessel or bronchial architecture (16,30) (**Fig 2**). This ability to safely counteract heat-sink effects likely led to our observed local recurrence rate of 8%, which compares well with those associated with RF ablation and surgery (12–14).

Cryoablation effectively treated even larger tumors that are difficult to manage. In our study, 60% of lung lesions (12 of 20), 56% of liver lesions (five of nine), and 68% of soft-tissue lesions (21 of 31) were 3 cm or larger. Overall, 63% of lesions were 3 cm or larger. In comparison, in studies of RF ablation for pulmonary masses, only 23%–30% of tumors 3 cm or larger were fully ablated (12,14). The mean survival for patients with incomplete necrosis from RF ablation was 8.7 months, compared with 19.7 months in cases of complete necrosis (12,14).

Although chemotherapy is the gold standard in the palliative care of mNSCLC, local tumor control plays a major role for quality of life in long-term treatment. A study on more than 700 patients who had received two or more previous chemotherapy regimens for advanced NSCLC (31) determined that survival and local control effectiveness diminished greatly with each subsequent regimen and resulted in a considerable increase in chemical toxicity. In addition, most patients undergoing second-line therapy will not be treated further because of the increased burden of morbidities and insignificant survival gains (3). In the present study, we assessed the complication rates of cryoablation procedures to elucidate any potential beneficial or harmful aspects of our technique on a patient's quality of life. Of 49 total procedures, 8% (n = 4) were associated with grade 3 or higher complications that required surgical intervention or increased hospital stay for observation or resulted in death. The death (ie, grade 5 complication) occurred within the 1-month window after MCA but was considered unrelated to the procedure. Therefore, more than 90% of procedures had only transient (ie, 2–3 d) impact on quality of life after MCA. The potential for reduction of chemotherapy/targeted therapy toxicities for oligometastatic NSCLC therefore appears much greater than the risks of procedural complications.

Cost-effectiveness estimates for this study were validated by a health economist with more than 30 years of experience (A.C.G.) (27), and were conducted to evaluate the economic impact of MCA in an adjunctive role by considering the added cost for palliation. We acknowledge that thorough cost-effectiveness estimates should include utility estimates for quality-adjusted life-years (QALY), as well as sensitivity analyses for probability and cost assumptions within the framework of a Markov or Monte Carlo decision model (22). Such in-depth analyses are beyond the scope of this study, which was focused on the feasibility, safety, and OS assessments of MCA for palliation in relation to potential cost-effectiveness.

Weaknesses in the present study relate to the relatively small patient population compared with large multicenter drug trials and the associated potential selection bias. Our study sample size was limited to patients with oligometastatic NSCLC to compare survival outcomes, but this precluded sufficient analyses of procedural details for pulmonary and/or soft-tissue cryoablation. Detailed assessments of progression-free survival were also beyond the scope of this study of local control. As noted, most of our patients had some form of initial chemotherapy or targeted therapy, which likely also improved OS duration. Also, although the definition of oligometastatic NSCLC varies in the medical literature, such lesions are generally considered less biologically aggressive (29). Patients with oligometastatic NSCLC may have survival potential greater than patients with traditional stage IV disease. Therefore, any survival gain in our patients with MCA may have been simply achieved by

Table 5. Preliminary Cost-effectiveness Estimates

Outcome	BSC	Erlotinib	Cisplatin/ Vinorelbine	Cisplatin/ Gemcitabine	Paclitaxel/ Cisplatin	Paclitaxel/Cisplatin/ Bevacizumab	MCA
LYGs	0.44	0.56	0.79	0.82	0.83	1.03	1.33
Total cost ($)*	5,581	16,487	15,564	13,517	18,709	56,209	59,600†
Cost per LYG ($)	12,684	29,441	19,701	16,484	22,541	54,572	44,812
ACER for adjunctive MCA‡							
Cost per LYG ($)	49,008	57,208	56,514	54,975	58,879	87,074	60,610§

Note.—Cost-effectiveness estimates for BSC and five established therapies (22–24) for mNSCLC are noted in conjunction with upper-bound estimates of cost for MCA. Our proposed ACER was used to calculate the estimated cost of MCA when paired with systemic regimens. ACER = adjunctive cost-effectiveness ratio, BSC = best supportive care, LYG = life-years gained, MCA = multisite cryoablation.

* Conversion factor of 1.67 from pounds to dollars was used to allow easier comparison and conforms to the difference between established definitions of cost efficacy of $100,000 (22,27).

† Assumes 1.6 cryoablation procedures per patient and more image intensive follow-up.

‡ ACER for the adjunctive role for MCA assumes costs are additive and divided by a total LYG of 1.33 for MCA.

§ Average cost per LYG.

selection rather than any MCA effect. Similarly, detailed assessments of morbidities were not feasible for the 84% of patients who received some form of chemotherapy/targeted therapy. It was interesting to find that the median survival in patients was longer in the patient group that received only BSC after MCA; however, this may not be an accurate assessment. Given that our study involved a relatively small patient pool, the improved survival in this group may be a result of a lower extent of disease aggressiveness/severity. Morbidity associated with chemotherapy/targeted regimens may also be a significant factor; however, we do not believe our limited data allow us to conclusively make such claims, but rather introduce a possible benefit of cryoablation in reducing chemotherapy toxicity. Nevertheless, the future assessment of potential reductions of chemotherapy toxicity by the use of MCA or other ablation modalities for oligometastatic NSCLC appears promising. Further work is needed to convert LYGs to QALYs for this adjunctive role of MCA, and in-depth procedural and periprocedural true cost assessments are also needed.

Our cost analyses were also limited. A more comprehensive "social" cost-effectiveness analysis would require enumeration of additional costs on the patient's end. These would include costs of travel to and from the treatment facility, foregone wages from lost work days, and incremental costs (if any) incurred by family members in the provision of treatment. Inclusion of these costs would increase the total cost estimates, yet would likely not contribute to our already upper-bound cost estimates. However, the social and economic impacts of the very low complication and tumor recurrence rates associated with MCA were also not considered for this study, but will likely favor conversion of LYGs to QALYs, especially in relation to chemotherapy toxicities.

In summary, percutaneous cryoablation of oligometastatic NSCLC appears well tolerated, with minimal morbidity and low local recurrence rates. This technique may extend OS beyond current systemic treatments alone. Future potential for reduction of chemotherapy toxicities by the use of MCA for oligometastatic NSCLC appears promising.

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