SBRT can be considered as a treatment option for patients with oligometastases.

Stereotactic Body Radiotherapy in the Management of Oligometastatic Disease
Kamran A. Ahmed, MD, and Javier F. Torres-Roca, MD

Background: The treatment of oligometastatic disease has become common as imaging techniques have advanced and the management of systemic disease has improved. Use of highly targeted, hypofractionated regimens of stereotactic body radiotherapy (SBRT) is now a primary management option for patients with oligometastatic disease.

Methods: The properties of SBRT are summarized and the results of retrospective and prospective studies of SBRT use in the management of oligometastases are reviewed. Future directions of SBRT, including optimizing dose and fractionation schedules, are also discussed.

Results: SBRT can deliver highly conformal, dosed radiation treatments for ablative tumors in a few treatment sessions. Phase 1/2 trials and retrospective institutional results support use of SBRT as a treatment option for oligometastatic disease metastasized to the lung, liver, and spine, and SBRT offers adequate toxicity profiles with good rates of local control. Future directions will involve optimizing dose and fractionation schedules for select histologies to improve rates of local control while limiting toxicity to normal structures.

Conclusions: SBRT offers an excellent management option for patients with oligometastases. However, additional research is still needed to optimize dose and fractionation schedules.

Introduction
The concept of the oligometastatic state in cancer management was first proposed in 1995 by Hellman and Weichselbaum, who hypothesized a subset of patients with metastatic disease presenting with limited metastatic disease that might be amenable to curative therapy. The validity of this concept has been demonstrated by multiple studies demonstrating long-term survival rates in a subset of patients when treated with aggressive local therapy, including surgery and radiotherapy.

Various radiation techniques have been used for the treatment of oligometastases. Use of high doses of single-session stereotactic radiosurgery has been employed in the management of brain metastases. Treatment with single-session stereotactic radiosurgery has also been extended to treat patients with at least 4 brain metastases (range, 4–18). A similar approach has been used with either a hypofractionated treatment regimen, decreasing the number of fractions delivered by increasing daily treatment doses, or single-session regimens with ablative doses of radiation delivered to extracranial disease sites.

The American Society of Radiation Oncology de-
fines stereotactic body radiotherapy (SBRT) as external-beam radiation used to precisely deliver high doses of radiation to an extracranial target within the body, either as a single dose or a small limited number of radiation fractions. The most studied and reported institutional experiences involve treatment to metastases in the lung, liver, and spine. In this review, we summarize the major studies reported in the management of oligometastatic disease and the management of lung, liver, and spine metastases with SBRT.

**Oligometastatic Disease**

Assessment of the oligometastatic state has historically been limited by imaging capabilities, and many patients previously treated for oligometastatic disease may have had underlying and undetected widespread metastases. Use of positron emission tomography/computed tomography has significantly improved the identification of patients with limited metastatic disease.10-12 Clinical experience has been significant in documenting the effectiveness of surgical resection as a treatment option for these patients. Reports have discussed surgery as the management option for lung metastases, metastases to the liver from colorectal primaries, and soft-tissue sarcoma metastases.2,3,13 In the management of lung metastases, surgery has produced good, long-term outcomes in the resection of renal, colorectal, sarcoma, and breast cancer histologies.14-17 Watanabe et al14 reported a 5-year survival rate of 68% following an R0 resection of colorectal metastases to the lung in 113 study patients. The 5-year survival rates in the resection of lung metastases of primary breast cancer have ranged from 36% to 54%, with a similar 5-year survival rate of 31% reported in the resection of 52 bone sarcoma pulmonary metastases.15,16 Other studies have reported results in the surgical management of liver metastases of colorectal primaries. In a review from Simmonds et al3 of 30 studies, they reported that the 5-year survival rate was approximately 30% and the postoperative mortality rates were relatively low (median rate, 2.8%). Thus, from the data of this surgical series, we can conclude that patients with both lung and liver metastases might achieve long-term survival with definitive surgical management.5

**Stereotactic Body Radiotherapy**

Historically, use of radiation for the treatment of metastatic disease was restricted to palliation. Radiation to areas of metastatic deposits has been limited by a balance of delivering truly ablative doses of radiation with the risks to surrounding normal tissues. In addition, the need for extended, prolonged fractionation schedules in patients with metastatic disease has limited the feasibility of conventional radiation treatment.9 The initial trials of SBRT were conducted on 42 tumors of the liver, lung, and retroperitoneal space in 31 study patients using mean doses of 8 to 66 Gy in 1 to 4 fractions, and the researchers reported a local control rate of 80% with a follow-up period of 1.5 to 38 months.18 With such high doses of radiation being delivered per fraction, patient immobilization to ensure accurate tumor targeting while limiting dose to normal structures is of paramount importance. This was achieved by a body frame holding the patient accompanied by a vacuum pillow to form a tight, reproducible seal around the patient.

Similar immobilization devices are used in the majority of SBRT treatments. Additional devices have been utilized to limit and track tumor motion in the treatment of lung and liver metastases. This has been achieved using 4-dimensional treatment planning software, allowing tumors to be tracked during the respiratory cycle and restricting treatments to particular phases of the respiratory cycle.19 Tumor motion due to respiratory excursion can also be restricted using abdominal compression, thus limiting motion of the diaphragm during treatment.20 Furthermore, daily set-up verification with cone-beam computed tomography helps to ensure adequate treatment positioning for each high dose of delivered treatment.21 Together, these treatment techniques ensure accurate tumor targeting while also limiting the dose to normal structures.

SBRT is typically delivered using gantry-based linear accelerators with multileaf collimators to shape the radiation treatment field. The treatment plan is created using a number of beams to increase the dose to the target while minimizing the dose delivered to normal tissues. SBRT is often the preferred radiation treatment option for sites of oligometastatic disease due to the limited radiation dose delivered to normal tissues with highly conformal treatment planning software and the limited number of fractions needed for treatment.

**Mixed Oligometastatic Sites**

The definition of oligometastatic disease has varied between studies. Milano et al5 defined persons with oligometastatic disease as those with no more than 5 detectable metastases. Salama et al4 similarly defined oligometastatic disease as 1 to 5 metastatic sites. However, other institutions have limited their eligibility for SBRT to patients with no more than 3 metastatic sites.22 Other patient factors taken into account to determine SBRT eligibility traditionally include performance status, primary rate of disease control, and life expectancy. Several studies have assessed outcomes in patients treated to mixed sites of oligometastatic disease in an effort to assess rates of local control, toxicity, and survival.5,23-26 The largest series to date of study patients treated to mixed sites of oligometastatic disease was published by Milano et al,5 who reported outcomes in 121 study patients treated with curative-intent SBRT. The majority of study patients were treated with
10 fractions of 5 Gy.5 The rates of 2-year overall survival (OS), progression-free survival (PFS), local control, and distant control were 50%, 26%, 67%, and 34%, respectively.5 The most common sites of metastases were in the lung, liver, and lymph nodes.5

Other groups have reported similar outcomes in the management of oligometastatic sites. For example, Salama et al4 reported on SBRT in 61 study patients with 113 metastases who had life expectancies longer than 3 months. This dose-escalation study initially treated participants with a rate of 24 Gy in 3 fractions and then sequentially increased the rate to 48 Gy in 3 fractions.4 No dose-limiting toxicities were seen in study patients treated to 48 Gy.4 The 1- and 2-year PFS rates were 33.3% (95% confidence interval [CI], 22.8–46.1) and 22.0% (95% CI, 12.8–34.4), respectively, and no significant response rate between dose levels was reported.4 Greco et al23 reported on outcomes in 126 metastases in 103 study patients treated with single-dose SBRT at doses ranging from 18 to 24 Gy. The most common primary histologies were prostate, renal, and colorectal, with the majority of treated sites in the bone, lymph nodes, and soft tissue.23 A dose-response relationship was noted, as was a 2-year local control rate of 64% (82% if > 22 Gy, 25% for 18–20 Gy).23

Taken together, these studies show treating patients with a limited number of metastases with SBRT is feasible and offers adequate PFS rates at 24 months.4,23 In addition, toxicity rates in these studies were acceptable, indicating SBRT is a safe alternative to surgical resection.4,23

A summary of studies of SBRT for mixed oligometastatic sites is included in Table 1.4,5,23-26

### Liver

Many studies have assessed SBRT in the control of metastases to the liver, and some prospective phase 1/2 trials have established the safety and efficacy of SBRT as a treatment modality for liver metastases.57-31 A summary of the prospective trials assessing SBRT for the management of liver metastases is reported in Table 2.27-31

Lee et al30 reported phase 1/2 outcomes in 68 inoperable or medically unsuitable study patients. Individualized radiation doses were chosen to maintain the same nominal risk of radiation-induced liver disease.30 The median SBRT dose was 41.8 Gy (range, 27.7–60 Gy) in 6 fractions over 2 weeks, and the most common histologies were colorectal (n = 40), breast (n = 12), or other (n = 16).30 SBRT was well tolerated: 6 (9%) acute grade 3 toxicities (gastrointestinal, nausea, lethargy, and thrombocytopenia) and 1 (1%) grade 4 toxicity (thrombocytopenia) were seen, and the 1-year local control rate was reported to be 71% (95% CI, 58–85).30 Rusthoven et al27 also reported phase 1/2 results in 47 study patients with 63 liver metastases with a maximal diameter less than 6 cm in a dose-escalation trial of 36 to 60 Gy in 3 fractions.27 No cases of radiation-induced liver disease were noted, but 1 study patient did experience grade 3 or higher toxicity (2%).27 Local control rates at 1 and 2 years following SBRT were 95% and 92%, respectively, with a median survival rate of 20.5 months.27

Although local control rates were higher in this study, the lesions were smaller, with a median volume

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Lesions</th>
<th>Dose</th>
<th>Rate of Local Control</th>
<th>Rate of Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greco23</td>
<td>126</td>
<td>18–24 Gy in 1 fraction</td>
<td>64% at 2 y</td>
<td>Grade 3 (&lt; 4%)</td>
</tr>
<tr>
<td>Kang25</td>
<td>78</td>
<td>42 Gy in 3 fractions</td>
<td>66% at 3 y</td>
<td>Grade 4 (3%)</td>
</tr>
<tr>
<td>Milano5</td>
<td>293</td>
<td>Median 50 Gy in 10 fractions</td>
<td>77% at 2 y</td>
<td>Grade 3 (1%)</td>
</tr>
<tr>
<td>Salama4</td>
<td>113</td>
<td>24–48 Gy in 3 fractions</td>
<td>67% at 2 y</td>
<td>Grade 3 Acute: 3% Late: 10%</td>
</tr>
<tr>
<td>Stinauer26</td>
<td>53</td>
<td>40–50 Gy in 5 fractions</td>
<td>88% at 18 mo</td>
<td>Grade 3 (3%)</td>
</tr>
<tr>
<td>Wersall24</td>
<td>162</td>
<td>30–40 Gy in 3 fractions</td>
<td>Crude (90%)</td>
<td>Grade ≥ 1 toxicity (40%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Lesions</th>
<th>Dose</th>
<th>Rate of Local Control</th>
<th>Rate of Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herfarth28</td>
<td>60</td>
<td>14–26 Gy in 1 fraction</td>
<td>81% at 18 mo</td>
<td>No major adverse events reported</td>
</tr>
<tr>
<td>Hoyer29</td>
<td>44</td>
<td>45 Gy in 3 fractions</td>
<td>86% at 2 y</td>
<td>1 death from hepatic failure Grade 4 (1) Grade 3 (2)</td>
</tr>
<tr>
<td>Lee30</td>
<td>68</td>
<td>Median 41.8 Gy in 6 fractions</td>
<td>71% at 12 mo</td>
<td>Grade 3 (6) Grade 4 (1)</td>
</tr>
<tr>
<td>Rusthoven27</td>
<td>63</td>
<td>60 Gy in 3 fractions</td>
<td>92% at 2 y</td>
<td>No grade 4/5</td>
</tr>
<tr>
<td>Scorsetti31</td>
<td>76</td>
<td>Majority 75 Gy in 3 fractions</td>
<td>94% at 12 mo</td>
<td>No grade ≥ 3</td>
</tr>
</tbody>
</table>
of 14.9 mL, compared with 75.2 mL in Lee et al.27,30 Nevertheless, these results raise the question of whether higher radiation doses for the management of liver metastases may improve local control rates.

A study by Hoyer et al29 reported on the results of inoperable colorectal metastases treated with SBRT in the liver (n = 44), lung (n = 12), lymph nodes (n = 3), suprarenal gland (n = 1), or 2 organs (n = 4) with a central dose of 15 Gy on 3 occasions within 5 to 8 days. The 2-year rates of local control by tumor and patient were 86% and 63%, respectively.29 Toxicities included 1 liver failure leading to death and 2 severe, late gastrointestinal toxicities.29 Despite these toxicities, the authors noted adequate toxicity profiles for the majority of study patients.29

Fig 1 is an example of a treatment plan for SBRT in a patient with a renal cell metastasis to the liver.

**Lung**

Historically, the standard of care for early stage non–small-cell lung cancer is surgical resection. Reports of treatment with SBRT represented a novel approach for the management of inoperable early stage lung cancer; the initial phase 1 data in patients with medically inoperable stage 1 disease were published by Timmerman et al.32 Doses ranged from 8 to 20 Gy in 3 fractions.32 Researchers of a phase 2 trial treated 59 study patients with medically inoperable stage T1/T2 N0 M0 non–small-cell lung cancer with 18 Gy for 3 fractions, reporting a 3-year local control rate of 98%.35

The pioneering work from Timmerman et al32 was eventually translated to the setting of oligometastatic disease and lung metastases.34-38 Ricardi et al34 published a series of 61 study patients with oligometastatic lung tumors. Dose selection was 26 Gy in 1 fraction in 51 study patients, 45 Gy in 3 fractions in 22 study patients, and 36 Gy in 4 fractions in 3 study patients.34 After a median follow-up interval of 20.4 months, local control rates at 2 and 3 years were 89% and 83.5%, respectively, OS rates at 2 and 3 years were 66.5% and 52.5%, respectively, and PFS rates at 2 and 3 years were 32.4% and 22.3%, respectively.34

Siva et al39 published a systematic review of the literature on oligometastatic disease to the lung treated with SBRT, assessing 334 study patients with 564 targets. The 2-year weighted local control rate was 77.9%, the corresponding 2-year weighted OS rate was 53.7%, and a 4% rate was seen of radiation toxicity of grade 3 or higher.39 In addition, the series reported on single-fraction stereotactic radiosurgery to 154 study patients treated to 174 targets, and the 2-year weighted rate of local control was 78.6%.39

No randomized data have yet to determine whether surgical resection and SBRT are equivalent treatment options for oligometastatic disease. Several trials have been attempted in the primary lung cancer setting, but they were closed due to poor accrual (NCT00687986, NCT00840749). However, SBRT is still an accepted approach for the management of lung metastases due to its efficacy, safety, and feasibility.

Fig 2 shows a lesion in the left upper lobe of the lung treated with 50 Gy in 5 fractions, and Table 3 sum-
marizes the studies evaluating the management of oligometastatic lung disease treated with SBRT.\textsuperscript{34-38}

**Spine**

In addition to its use in the setting of reirradiation and radioresistant histologies, SBRT to the spine is indicated for the treatment of oligometastatic disease.\textsuperscript{40,41} Many prospective and retrospective series have reported outcomes in the management of spinal metastases with SBRT.\textsuperscript{22,41-46} A summary of reported series on SBRT to the spine are reported in Table 4.\textsuperscript{22,41-46}

A phase 1/2 trial of 149 study patients with 166 lesions were treated with SBRT to the spine, receiving total doses of 27 to 30 Gy, typically in 3 fractions.\textsuperscript{42} The number of study patients reporting no pain from bone metastases, as measured by the Brief Pain Inventory, increased from 39 (26%) prior to SBRT to 55 (54%) 6 months after SBRT (\(P < .0001\)).\textsuperscript{42} They were followed for a median of 15.9 months and had a local control rate of 72%.\textsuperscript{42}

The largest report to date of SBRT to the spine was a retrospective review from Gerszten et al,\textsuperscript{45} who reported the results of 393 study patients with mixed histology (500 total lesions). No significant neurological effects were reported.\textsuperscript{45} The researchers followed the study patients for a median of 21 months and reported a tumor control rate of 88%.\textsuperscript{45}

Zelefsky et al\textsuperscript{41} reported a significant dose-response relationship in the management of renal cell carcinoma metastases to the spine. Renal cell carcinoma has traditionally been thought to be radioresistant, so Zelefsky et al\textsuperscript{41} indicated a higher biological effective dose may be necessary to achieve adequate tumor control.\textsuperscript{41} With a dose of 24 Gy in 1 fraction, a 3-year PFS rate of 88% was achieved with a rate of 21% for a dose lower than 24 Gy in 1 fraction.\textsuperscript{41} These results are intriguing and should be assessed further in randomized prospective trials.

Although a significant dose-response relationship

![Fig 2. — (A) Three-dimensional reconstruction and (B) axial, (C) sagittal, and (D) coronal imaging for a lesion in the left upper lobe of the lung treated with 50 Gy in 5 fractions.](image)

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Lesions</th>
<th>Dose</th>
<th>Rate of Local Control</th>
<th>Rate of Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Okunieff\textsuperscript{37}</td>
<td>125</td>
<td>50 Gy in 10 fractions (most common)</td>
<td>91% at 3 y</td>
<td>Grade 2 (6.1%) Grade 3 (2%)</td>
</tr>
<tr>
<td>Onimaru\textsuperscript{38}</td>
<td>57</td>
<td>48–60 Gy in 8 fractions</td>
<td>70% at 3 y for 48 Gy 100% for 60 Gy</td>
<td>Grade 5 (2.2%)</td>
</tr>
<tr>
<td>Ricardi\textsuperscript{34}</td>
<td>77</td>
<td>26 Gy in 1 fraction to 45 Gy in 3 fractions</td>
<td>89% at 2 y</td>
<td>Grade 3 (1.6%)</td>
</tr>
<tr>
<td>Rusthoven\textsuperscript{36}</td>
<td>63</td>
<td>60 Gy in 3 fractions</td>
<td>96% at 2 y</td>
<td>Grade 3 (8%)</td>
</tr>
<tr>
<td>Yoon\textsuperscript{35}</td>
<td>101</td>
<td>30 Gy in 3 fractions to 48 Gy in 4 fractions</td>
<td>70% for 30 Gy 77% for 40 Gy 100% for 48 Gy</td>
<td>No cases of grade ≥ 2</td>
</tr>
</tbody>
</table>
was reported by Zelefsky et al., caution must be taken to avoid any excess dose to the spinal cord, which could lead to acute and late toxicities. Fig 3 shows a radiation therapy plan for T11 metastases due to leiomyosarcoma that were treated with 25 Gy in 5 fractions and dose painting to 30 Gy to areas of gross disease. Dose constraints to the spinal cord have included a maximum dose of less than 22 Gy, less than 0.35 cc receiving 18 Gy, and less than 1.2 cc receiving 12.3 Gy. Radiation oncologists must cautiously select candidates for SBRT of the spine to avoid additional risks to the spine that can occur with SBRT compared with conventional external-beam radiotherapy. Following conventional external-beam radiotherapy, the risk of vertebral compression fractures has been reported to be 5%; however, several retrospective series have reported higher rates of vertebral compression fractures with SBRT (11%–39%). Decreased dose to the spinal cord can be achieved using conformal radiation treatment planning. However, myelopathy continues to be a rare but significant toxicity; the largest reported series of 1,075 study patients reported this rate to be 0.6%. Particular attention must be taken to decrease dose delivery to the spinal cord, particularly in the setting of reirradiation, to minimize the risk of myelopathy.

**Factors Affecting Outcomes**

Increasing clinical evidence suggests that the management of oligometastases should differ based on primary histology. A study from Takeda et al. suggested that clinical outcomes may be different between the local control of oligometastatic lung lesions and primary lung cancers. Their study assessed 21 colorectal metastatic lung lesions, 23 lesions from other origins, and 188 primary lung cancers treated with 50 Gy in 5 fractions. On multivariate analysis, they found that the origin of the tumor was significant ($P < .05$). The researchers reported 1-year local control rates of 80%, 94%, and 97% ($P < .05$) for colorectal primaries, oligometastases from other origins, and clinically diagnosed lung cancer, respectively. For the management of oligometastatic disease, Milano et al. found differences in the outcomes of local control rates depending on breast primaries vs non-breast primaries with 2-, 4-, and 6-year local control rates of 87% for breast primaries and 74%, 68%, and 65% for non-breast primaries, respectively.
Taken together, these data indicate histology is a variable that might affect outcomes and should be taken into account when developing SBRT dosing and fractionation schedules.

**Formula for the Biological Effective Dose**

The biological effective dose delivered to a tumor is a mathematical formula based on the linear quadratic model. The formula helps estimate the biological effect of a delivered dose to a tumor, taking into account the number of radiation treatments, the total dose delivered, and the α:β ratio. The α:β ratio is used to describe the curvature of the cell survival curve after radiation. Low α:β ratios characterize late-responding tissues and high α:β ratios delineate early-responding tissues. The formula is given as:

\[
\text{Biological effective dose} = nd \left(1 + \frac{d}{\alpha:\beta}\right)
\]

In this formula, \(n\) is the number of fractions and \(d\) is the dose per fraction.

Assuming an α:β ratio of 10, we can see 3000 cGy in 1 fraction vs 3000 cGy in 10 fractions would predict the biological effective doses to be:

<table>
<thead>
<tr>
<th>Dose Configuration</th>
<th>Effective Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 Gy × 1</td>
<td>30(1 + 3.0) = 120</td>
</tr>
<tr>
<td>3.0 Gy × 10</td>
<td>30(1 + 0.30) = 39</td>
</tr>
</tbody>
</table>

Using this biological effective dose model, we can see the higher biological dose delivered using SBRT doses.

However, the linear quadratic model has limitations when assessing high-dose fractionation regimens. The α:β ratio in the linear quadratic model depends on the dose range, and parameters used for conventional fractionation cannot be applied to high dose-per-fraction situations. In addition, it fails to predict tumor or normal-tissue responses at high doses based on conventional radiotherapy experiences. Additional models, such as the generalized linear quadratic model suggested by Wang et al., may be better suited to assess the conversion of sublethal to lethal DNA damage with SBRT and high-dose-rate brachytherapy. However, because no consistent model has been developed to measure the biological effect of larger hypofractionated SBRT dosages, radiation oncologists have had difficulty developing dose-fractionation regimens for SBRT and high-dose radiation brachytherapy to model biological effect.

**Dose Selection**

Various dosing schedules have been suggested for both lung and liver metastases. However, an optimal dosing schedule that takes into account factors such as lesion volume, primary histology, and biological response has yet to be determined. Data from McCammon et al. suggest a dose-response relationship in the treatment of liver and lung metastases. They reported on 246 lesions treated with SBRT for 3 fractions and lesions treated to a dose of at least 54 Gy and found 3-year local control rates of 89.3% compared with 59.0% and 8.1% for those treated to between 36 and 53.9 Gy and less than 36 Gy, respectively. Fumagalli et al. suggested a difference in outcome based on anatomical location. They assessed outcomes in hepatic or pulmonary oligometastases, of which 70% were digestive primary, and an improved disease-free survival rate on univariate analysis was noted in study patients with pulmonary metastases (\(P = .02\)). Results from these groups suggest a difference may exist in SBRT outcomes based on treatment location and that dose selection plays an important role in achieving optimum control.

**Future Directions of the Radiosensitivity Index**

Differences exist in the radiosensitivity of tumors based on the α:β ratio of the cell survival curve. We previously developed the radiosensitivity index (RSI) modeled as a function of gene expression, tissue of origin, Ras, and p53 status correlated to the surviving fraction of cells at 2 Gy in a panel of 48 human cancer cell lines. In another study, we assessed RSI differences between primary and metastatic colon cancers. As suggested by the clinical experience of other groups using SBRT, we found significant differences in RSI based on the anatomical location of metastases.

Our clinical practice has been to treat both lung and liver metastases regardless of primary histology to 60 Gy in 5 fractions of SBRT. Assessing our own institutional experience with the management of lung and liver metastases with primary colon cancer, we have found significant differences in local control outcomes, with lung metastases faring better than liver metastases. This correlates well to our RSI analysis, which revealed liver metastases of primary colon cancer to be more radioresistant than those of lung metastases. Thus, we propose that RSI could be used as a model to select dose and fractionation schedules for various anatomical sites and various histologies, possibly setting the stage for use in future clinical trials.

**Conclusions**

As novel, targeted agents are developed and systemic disease control is improved, local control of oligometastatic disease will become more important. Many
prospective and retrospective studies have revealed stereotactic body radiotherapy (SBRT) to be a safe management option for the control of oligometastatic disease to various disease sites with good local control.22,41-45 Due to the shortened time course and ablative radiation doses, SBRT is ideal for the management of metastatic cancer with limited sites of disease.

The optimal dose and fractionation schedule of SBRT for various sites of disease have yet to be determined. Increasing evidence suggests a uniform treatment schedule cannot be applied to all metastases, and dosing and fractionation schedules must be individualized based on tumor histology and anatomical location. As we move toward an era of personalized medicine, it will become increasingly important that dose and fractionation schedules be tailored to specific tumors.

References


