New concepts and insights regarding the role of radiation therapy in metastatic disease

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Radiation Oncology

Palliative radiotherapy in lung cancer

- Locally advanced disease
- Patients unfit for radical treatment
- Stage and Tumor burden
- Metastatic disease
  - Brain metastases
  - Bone metastases (spinal cord compression)
  - Pulmonary metastases
  - Adrenal gland metastases
  - Liver metastases
Brain metastases: background

Increasing incidence over time, due to:

- improved detection by enhanced diagnostic imaging
- aging population
- better treatment of systemic disease
- more effective therapies for treating primary tumors lengthening patients’ survival

Brain metastases: background

- Multiple brain metastases are present in as much as 60-70% of the patients
- Radiotherapy, especially with the great technical development during the past decades, represents a cornerstone of current treatment options
- Despite advances in treatment options, the prognosis is still poor
Brain metastases and prognosis

Survival by RPA prognostic group

Gaspar et al, 1997

Brain metastases: background

- Many patients affected with brain metastases die as a result of extra-cranial disease progression
- A substantial number of brain metastases patients suffer from the local tumor progression in the CNS
- Optimising local control is thus of paramount importance
Brain metastases: background

- Treatment decisions must be individualized based on a complex array of both patient-specific and tumor-specific characteristics

### Recursive Partitioning Analysis

<table>
<thead>
<tr>
<th>Class</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Age &lt;65 y, KPS &gt; 70, controlled primary tumor, no extracranial metastases</td>
</tr>
<tr>
<td>II</td>
<td>All patients not in Class I or III</td>
</tr>
<tr>
<td>III</td>
<td>KPS &lt; 70</td>
</tr>
</tbody>
</table>

### Graded Prognostic Assessment

<table>
<thead>
<tr>
<th>Score</th>
<th>0</th>
<th>0.5</th>
<th>1.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>&gt;40</td>
<td>&lt;50</td>
<td>&lt;50</td>
</tr>
<tr>
<td>KPS</td>
<td>&lt;50</td>
<td>50-90</td>
<td>90-100</td>
</tr>
<tr>
<td>No. of CNS metastases</td>
<td>&gt;3</td>
<td>2-3</td>
<td>1</td>
</tr>
<tr>
<td>Extracranial metastases</td>
<td>Present</td>
<td>–</td>
<td>None</td>
</tr>
</tbody>
</table>

Table 1. Recursive partitioning analysis

Table 4. Graded Prognostic Assessment
Treatment of brain metastases

- Number of lesions
- Size and site of lesions
- Status of extracranial disease

Multiple Brain Metastases

Whole Brain Radiotherapy
**WBI for Multiple Brain Metastases**

- WBI is the conventional treatment for majority of patients affected with (symptomatic) brain mets

- Typical radiation schedule: 30 Gy/10 fr
  
  37.5 Gy/15 fr (RTOG)

**Brain metastases**

Role of Radiosurgery, # mets
Review of randomized clinical trials in brain metastases

RCT in oligometastatic patients

WBRT alone vs WBRT + Radiosurgery

<table>
<thead>
<tr>
<th>Author</th>
<th>Treatment</th>
<th>Prescribed dose</th>
<th>n</th>
<th>Inclusion criteria</th>
<th>Mean control</th>
<th>Freedom from new brain metastases</th>
<th>Brain control</th>
<th>Neurologic death</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kondziolka [12]</td>
<td>WBRT: 30 Gy in 10 f</td>
<td>2-4 lesions, all the primaries</td>
<td>27</td>
<td>a.a.</td>
<td>6 m</td>
<td>34 m</td>
<td>a.a.</td>
<td>NS</td>
<td>66%</td>
</tr>
<tr>
<td>Andrews [13]</td>
<td>WBRT: 30.5 Gy in 15 f</td>
<td>1-3 lesions, all the primaries</td>
<td>131</td>
<td>a.a.</td>
<td>34 m</td>
<td>34 m</td>
<td>a.a.</td>
<td>NS</td>
<td>51.0%</td>
</tr>
</tbody>
</table>

S. surgery; WBRT, whole brain radiotherapy; RS, radiosurgery; f, fractions; h, hours; d, days; w, weeks; m, months; y, year; a.a. not available; NS, not statistically significant difference; BM, brain metastases.
**RCT in oligometastatic patients**

**Exclusive local treatment (surgery or radiosurgery) vs WBRT + local treatment (surgery or radiosurgery)**

<table>
<thead>
<tr>
<th>Author</th>
<th>Treatment arms</th>
<th>Prescribed dose</th>
<th>n</th>
<th>Inclusion criteria</th>
<th>Freedom from new brain metastases</th>
<th>Brain tumor control</th>
<th>Neurologic death rate</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patchell [14]</td>
<td>S = -</td>
<td>WBRT: 70.4 Gy in 28 fr</td>
<td>95</td>
<td>Single lesion</td>
<td>54.0%</td>
<td>90.0%</td>
<td>90.0%</td>
<td>44.0% NS</td>
</tr>
<tr>
<td></td>
<td>S + WBRT</td>
<td>WBRT: 70.4 Gy in 28 fr</td>
<td></td>
<td>All the primaries</td>
<td>19.0%</td>
<td>90.0%</td>
<td>82.0%</td>
<td>14.0% NS</td>
</tr>
<tr>
<td>Ayusse [15]</td>
<td>RS</td>
<td>RS ≤ 2 cm: 22–25 Gy, 2 cm: 18-20 Gy</td>
<td>77</td>
<td>1–3 lesions, All the primaries</td>
<td>72.5%</td>
<td>64.6%</td>
<td>68.6%</td>
<td>33.6% NS</td>
</tr>
<tr>
<td></td>
<td>RS + WBRT</td>
<td>RS ≤ 2 cm: 22–25 Gy, 2 cm: 18-20 Gy</td>
<td></td>
<td>67.0%</td>
<td>100.0%</td>
<td>73.0%</td>
<td>73.0%</td>
<td>5.7% NS</td>
</tr>
<tr>
<td>Chang [16]</td>
<td>RS</td>
<td>RS ≤ 2 cm: 18 Gy, 2-3 cm: 15 Gy; 3-4 cm: 12 Gy</td>
<td>58</td>
<td>1-3 lesions, All the primaries</td>
<td>67.0%</td>
<td>45.0%</td>
<td>77.0%</td>
<td>15.2% NS</td>
</tr>
<tr>
<td></td>
<td>RS + WBRT</td>
<td>RS ≤ 2 cm: 18 Gy, 2-3 cm: 15 Gy; 3-4 cm: 12 Gy</td>
<td></td>
<td>67.0%</td>
<td>100.0%</td>
<td>73.0%</td>
<td>73.0%</td>
<td>5.7% NS</td>
</tr>
<tr>
<td>Mueller and</td>
<td>RS or S</td>
<td>WBRT: 70.4 Gy in 28 fr</td>
<td>19</td>
<td>Single lesion All the primaries</td>
<td>67.0%</td>
<td>62.6%</td>
<td>62.6%</td>
<td>28.0% NS</td>
</tr>
<tr>
<td>Kocher [20]</td>
<td>RS or S</td>
<td>WBRT: 70.4 Gy in 28 fr</td>
<td></td>
<td>67.0%</td>
<td>100.0%</td>
<td>73.0%</td>
<td>73.0%</td>
<td>5.7% NS</td>
</tr>
</tbody>
</table>

S, surgery; WBRT, whole brain radiotherapy; RS, radiosurgery; fr, fraction; w, weeks; m, months; y, year; n.a., not available; NS, not statistically significant difference.

**Summary review:**

Radiotherapy and Oncology 102 (2012) 168-179

Treatment of brain metastases: Review of phase III randomized controlled trials

*Data from Reference 13, Nigro et al.*

Review of randomized clinical trials in brain metastases
Review of randomized clinical trials in brain metastases
Neurocognition Balance

- WBRT reduces intracranial relapse and prolongs time to relapse
  - This should preserve NCF or slow down its decline, as tumor progression is associated with NCF decline
- WBRT damages the brain
  - This should cause an early decline in brain function

So, where is the balance
HRQOL evaluation: EORTC QOL-C30 and BN-20 module

The primary HRQOL endpoint was global QoL; the secondary HRQOL endpoints were Cognitive, Physical, Emotional, Role Functioning and Fatigue.

88% basal evaluation; 51% @ 6 months; 45% @ 12 months

Statistical significance required \( p \leq 0.05 \) and clinical relevance \( \geq 10 \) pt difference

R. Soffietti, ASCO 2010

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### EORTC 22952-26001

**Quality of Life results of an EORTC phase III randomized trial of adjuvant Whole Brain Radiotherapy versus Observation after Radio surgery or Surgical Resection of 1-3 Cerebral Metastases of solid tumors**

**HRQoL results**

- Timepoint: Baseline, 8 wks, 3 mths, 6 mths, 9 mths, 12 mths, Overall post baseline
- WBI Estimate (Std.Err.): WBI and No WBI
- Treatment difference
- p-value

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>WBI Estimate (Std.Err.)</th>
<th>No WBI Estimate (Std.Err.)</th>
<th>Treatment difference</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>58.3 (1.8)</td>
<td>60.0 (1.8)</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>8 wks</td>
<td>54.9 (2.1)</td>
<td>56.8 (2.2)</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>3 mths</td>
<td>58.0 (2.4)</td>
<td>58.6 (2.5)</td>
<td>0.9</td>
<td></td>
</tr>
<tr>
<td>6 mths</td>
<td>58.7 (2.9)</td>
<td>62.1 (2.9)</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>9 mths</td>
<td>52.2 (3.2)</td>
<td>63.2 (3.2)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>12 mths</td>
<td>56.8 (3.9)</td>
<td>58.7 (3.5)</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>Overall post baseline</td>
<td>0.1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**Results: Global health status / QoL**

- Global health status: Mean + 95% CI
- Time since (RadioSurgery)
- Treatment: Treatment, No WBR, WBR

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Review of randomized clinical trials in brain metastases

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Randomized Controlled Trials and neurocognitive evaluation

- Nearly all patients with brain metastases have some degree of baseline neurocognitive impairment, whereas brain progression is the most important factor in determining cognitive deterioration.

- Although the evidence of WBRT-related neurotoxicity of a clinically significant degree is arguable, the risk of long-term effects of WBRT on neurocognitive function cannot be excluded.
Hippocampal avoidance and WBI

Why avoid the hippocampus? A comprehensive review
Vini Gondi, Wolfgang A. Tome, Minesh P. Mehta

RADIATION THERAPY ONCOLOGY GROUP
RTOG 0933
A PHASE II TRIAL OF HIPPOCAMPAL AVOIDANCE DURING WHOLE BRAIN RADIOTHERAPY FOR BRAIN METASTASES

SCHEMA (12/5/11)

For Patients with MRI Evidence of Brain Metastasis Within 1 Month Prior to Registration

<table>
<thead>
<tr>
<th>Prior to Treatment Start</th>
<th>Radiation Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. MRI with Fused CT Simulation</td>
<td></td>
</tr>
<tr>
<td>2. Neurocognitive Function Testing</td>
<td></td>
</tr>
<tr>
<td>3. Quality of Life Assessment</td>
<td></td>
</tr>
<tr>
<td>4. Rapid Central Review of Hippocampal Contours and HA-WBRT Treatment Plan</td>
<td></td>
</tr>
<tr>
<td>WBRT with Hippocampal Avoidance using IMRT (30 Gy in 10 Fractions)</td>
<td></td>
</tr>
</tbody>
</table>
THE OLIGOMETASTATIC STATE

BACKGROUND

- In a 1995 JCO Editorial, clinical evidence led Hellmann and Weichselbaum to coin the term “oligometastases”
- In this paradigm, a sort of “intermediate” metastatic state peculiarly situated between loco regionally-confined and widely-metastatic cancer is postulated, in which malignant cells have not acquired the metastatic potential yet
- In such a state of disease burden, the underlying hypothesis is that the eradication of all sites of metastatic disease could result in long-term survival in a subgroup of patients

Stereotactic Body Radiation Therapy (SBRT)

An external beam radiation therapy method used to very precisely deliver a high dose of radiation to an extracranial target within the body, using either a single dose or a small number of large fractions

- Specialized treatment planning results in high target dose and steep dose gradients beyond the target
- The challenge is to hit the entire extent of the tumor with extremely potent and biologically damaging therapy, while simultaneously avoiding surrounding normal tissue (tumor ablation and normal tissues sparing)
THE OLIGOMETASTATIC STATE

LOCAL THERAPIES: SBRT

• No randomized data are available, but only phase I-II studies.

• A proper comparison between the published studies is hampered mainly by the different selection criteria and the widely variable fractionation schedules.

• When treating metastatic patients (even if “oligometastatic”), selection criteria are a pivotal issue. In general, clinical indications are the same as those for metastasectomy, but without the limits regarding patients unfit for surgery.
Spine Radiosurgery: Introduction

- The median duration of pain response after conventional palliative radiotherapy is approximately 3 to 6 months, again without differences between different fractionation schedules (poorer outcome for unfavorable histologies)
- This brief palliative effect may be sufficient for some patients with very short life expectancy
- As modern chemotherapy may further prolong life expectancy, long-term palliation and long-term tumor control become even more important goals
- Large interest in intensification of radiotherapy for painful vertebral metastases
Spine Radiosurgery: Introduction

- Stereotactic radiosurgery (1 to 5 fractions) has emerged as a new treatment option for the multidisciplinary management of metastases located within or adjacent to vertebral bodies and the spinal cord.

- Stereotactic radiosurgery uses image-guidance to deliver high-dose radiation precisely, creating a steep dose gradient at the interface between tumor and spinal cord.
Rationale for Spine Radiosurgery
(compared to conventional RT)

- More durable pain control and better long-term local tumor control
- More rapid pain relief
- Radioresistant histologies
- Better patient convenience
- Improvement of survival in oligometastatic setting

Patients selection?
Can we correctly estimate the prognosis of patients with bone metastases?

Modified Bauer scoring system for patients with spinal metastases

<table>
<thead>
<tr>
<th>Prognostic score*</th>
<th>Treatment goal</th>
<th>Surgical strategy</th>
<th>Median survival (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–1</td>
<td>Supportive care</td>
<td>No surgery</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>Short-term palliation</td>
<td>Dorsal</td>
<td>9</td>
</tr>
<tr>
<td>3–4</td>
<td>Middle term local control</td>
<td>Ventral-dorsal</td>
<td>17</td>
</tr>
</tbody>
</table>

* Positive scores for prognostic factors are: 1 point for no visceral metastases; 1 point for no lung cancer; 1 point for primary tumor, e.g., breast, kidney, lymphoma, multiple myeloma, and 1 point for one solitary skeletal metastasis (<5).
Prognostic Factors and a Scoring System for Survival After Radiotherapy for Metastases to the Spinal Column

Masashi Mizumoto, MD

Prognostic Factor
Type of primary tumor
  Favorable* 0
  Unfavorable 3
E.C.O.G. PS 3
Visceral metastases 2
Previous chemotherapy 2
Hypothyroidism 1
Multiple bone metastases 1
HIV (≤21 y) 1

ECOG PS indicates Eastern Cooperative Oncology Group performance status.
*Breast, prostate, lymphoma, and renal cancer (except anaplastic cancer)

CANCER  November 15, 2008 / Volume 113 / Number 10

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CLINICAL INVESTIGATION

RECURSIVE PARTITIONING ANALYSIS INDEX IS PREDICTIVE FOR OVERALL SURVIVAL IN PATIENTS UNDERGOING SPINE STEREOTACTIC BODY RADIATION THERAPY FOR SPINAL METASTASES


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Review of randomized clinical trials in brain metastases
Recursive partitioning analysis (RPA) for spinal SBRT

Time from Primary Diagnosis
n=174

>30 Month
n=86

≤30 Months
n=88

Group 1
KPS >70
n=59

Group 2
KPS ≤70
n=27

Group 2
Age <70
n=77

Group 3
Age ≥70
n=11

Overall Survival

Group 1 (n=59, MST=21.1 mo)
Group 2 (n=104, MST=8.7 mo)
Group 3 (n=11, MST=2.4 mo)

Group 1 = Time from Primary Dx >30 mo and KPS >70
Group 2 = Time from Primary Dx >30 mo and KPS ≤70 or Time from Primary Dx ≤30 mo and Age <70
Group 3 = Time from Primary Dx ≤30 mo and Age ≥70
Spine RS: Optimal patients

- Small-volume skeletal metastasis
- Limited metastatic tumor burden
- Good performance status

Review and Uses of Stereotactic Body Radiation Therapy for Oligometastases

**Filippo Alongi, Stefano Arcangeli, Andrea Riccardo Filippi, Umberto Ricardi, Marta Scorsetti**

<table>
<thead>
<tr>
<th>Study</th>
<th>n of patients</th>
<th>Medium dose/ n of fractions</th>
<th>Median follow-up, mos</th>
<th>Local control rate</th>
<th>Pain response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yamashita et al. [73]</td>
<td>93</td>
<td>24 Gy/1</td>
<td>15</td>
<td>15-mo, 90% (imaging)</td>
<td>NS</td>
</tr>
<tr>
<td>Ryu et al. [74]</td>
<td>49</td>
<td>10–16 Gy/1</td>
<td>6.4</td>
<td>93% (imaging and pain)</td>
<td>85%</td>
</tr>
<tr>
<td>Subgatk et al. [56]</td>
<td>14</td>
<td>24 Gy/3</td>
<td>9</td>
<td>78% (imaging and/or pain)</td>
<td>NS</td>
</tr>
<tr>
<td>Nguyen et al. [75]</td>
<td>25</td>
<td>24 Gy/3</td>
<td>7</td>
<td>92% (imaging and/or pain)</td>
<td>NS</td>
</tr>
<tr>
<td>Nguyen et al. [75]</td>
<td>48</td>
<td>30 Gy/5</td>
<td>13.1</td>
<td>78% (imaging)</td>
<td>52%</td>
</tr>
<tr>
<td>Tsai et al. [76]</td>
<td>69</td>
<td>15.5 Gy/2</td>
<td>10</td>
<td>10-mo, 96.8% (imaging)</td>
<td>Improved pain control, 88%</td>
</tr>
<tr>
<td>Chang et al. [58]</td>
<td>63</td>
<td>30 Gy/5</td>
<td>21.3</td>
<td>77% (imaging)</td>
<td>Narcotic use declined 66% to 36%</td>
</tr>
<tr>
<td>Gibbs et al. [77]</td>
<td>74</td>
<td>14–25 Gy/1–3</td>
<td>9</td>
<td>NS</td>
<td>Clinical benefit, 84%</td>
</tr>
<tr>
<td>Gerzzen et al. [78]</td>
<td>393</td>
<td>20 Gy/1</td>
<td>21</td>
<td>88% (imaging)</td>
<td>Clinical benefit, 86%</td>
</tr>
</tbody>
</table>

*The Oncologist* 2012;17:000–000  www.TheOncologist.com
Spine RS: Results

- Overall pain control rate: 70-90%
- Pain is reported to decrease usually within weeks after RS, and occasionally within days
- Radiographic tumor control rates are reported to be approximately 80-90%
Symptomatic cord compression: contraindication

Guckenberger et al. Radiat Oncol 2011, 6:172
http://www.ro-journal.com/content/6/1/172

Clinical practice of image-guided spine radiosurgery - results from an international research consortium

Matthias Guckenberger¹, Reinhart A Sweeney¹, John C Flickinger²,³, Peter C Gerszten⁴, Ronald Kersh⁵,⁶, Jason Sheehan⁷ and Arjun Sahgal⁸

Review of randomized clinical trials in brain metastases
Table 3  Guidelines for spinal SRS bony CTV delineation

<table>
<thead>
<tr>
<th>GTV involvement</th>
<th>ISRC GTV anatomic classification</th>
<th>ISRC bony CTV recommendation</th>
<th>CTV description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any portion of the vertebral body</td>
<td>1</td>
<td>1</td>
<td>Include the entire vertebral body</td>
</tr>
<tr>
<td>Lateralized within the vertebral body</td>
<td>1</td>
<td>1, 2</td>
<td>Include the entire vertebral body and the ipsilateral pedicle/transverse process</td>
</tr>
<tr>
<td>Diffusely involves the vertebral body</td>
<td>1</td>
<td>1, 2, 6</td>
<td>Include the entire vertebral body and the bilateral pedicles/transverse processes and bilateral laminae</td>
</tr>
<tr>
<td>GTV involves vertebral body and unilateral pedicle</td>
<td>1, 2</td>
<td>1, 2, 3</td>
<td>Include entire vertebral body, ipsilateral transverse process, and ipsilateral laminae</td>
</tr>
<tr>
<td>GTV involves vertebral body and bilateral pedicles/transverse processes</td>
<td>3</td>
<td>2, 3, 4</td>
<td>Include entire vertebral body, bilateral pedicles/transverse processes, and bilateral laminae</td>
</tr>
<tr>
<td>GTV involves unilateral pedicle</td>
<td>2</td>
<td>2, 3 ± 1</td>
<td>Include pedicle, ipsilateral transverse process, and ipsilateral lamina, ± vertebral body</td>
</tr>
<tr>
<td>GTV involves unilateral lamina</td>
<td>3</td>
<td>2, 3, 4</td>
<td>Include lamina, ipsilateral pedicle/transverse process, and spinous process</td>
</tr>
<tr>
<td>GTV involves spinous process</td>
<td>4</td>
<td>3, 4, 5</td>
<td>Include entire spinous process and bilateral laminae</td>
</tr>
</tbody>
</table>

Abbreviations: CTV = clinical target volume; GTV = gross tumor volume; ISRC = International Spine Radiosurgery Consortium.
Spine Radiosurgery Program

- Close cooperation between radiation oncologists and neurosurgeons, especially in patients with epidural disease, spinal cord compression and instability
- Limitations of the target volume to maximum 2-3 vertebras
- Dedicated imaging protocols for target and organ-at-risk definition
- Anatomical target volume concepts with proper safety margins
- Highly conformal treatment planning, daily image-guidance, thorough patient immobilization and intra-fraction patient monitoring
- Close follow-up with repeated clinical and radiological response evaluation
Review and Uses of Stereotactic Body Radiation Therapy for Oligometastases

FILIPPO ALONGI, a STEFANO ARCANGELI, a ANDREA RICCARDO FILIPPI, b UMBERTO RICARDI, b MARTA SCORSETTI b

<table>
<thead>
<tr>
<th>Study</th>
<th>n of patients</th>
<th>Median dose/median of fractions</th>
<th>Median (range) follow-up, mos</th>
<th>Local control rate</th>
<th>Overall survival</th>
<th>Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Casamassima et al. [26]</td>
<td>48</td>
<td>36 Gy/3</td>
<td>16.5 (3–63)</td>
<td>1–2 yr, 90%</td>
<td>1-yr, 39.7%; 2-yr, 14.5%</td>
<td>1 case of grade II adrenal insufficiency</td>
</tr>
<tr>
<td>Chawla et al. [24]</td>
<td>30</td>
<td>40 Gy/10</td>
<td>9.8 (3.2–28.3)</td>
<td>1-yr, 55%</td>
<td>1-yr, 44%; 2-yr, 25%</td>
<td>Mild grade 1 fatigue and nausea, “common”</td>
</tr>
<tr>
<td>Oshino et al. [25]</td>
<td>19</td>
<td>45 Gy/10</td>
<td>11.3 (5.4–87.8)</td>
<td>Objective response rate, 68%</td>
<td>1-yr, 59%; 2-yr, 33%; 3-yr, 22%</td>
<td>1 grade 2 dermatomal ulcer</td>
</tr>
<tr>
<td>Holy et al. [54]</td>
<td>18</td>
<td>20 Gy/5 or 40 Gy/8</td>
<td>21</td>
<td>Objective response rate, 77%</td>
<td>Median, 23 mos</td>
<td>–</td>
</tr>
<tr>
<td>Terok et al. [55]</td>
<td>7</td>
<td>16 Gy/1 or 27/3</td>
<td>14 (1–69)</td>
<td>1-yr, 63%</td>
<td>Median, 8 mos</td>
<td>–</td>
</tr>
</tbody>
</table>

Adrenal glands

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CLINICAL INVESTIGATION

STEREOTACTIC BODY RADIOTHERAPY FOR TREATMENT OF ADRENAL METASTASES

SHEELA CHAWLA, M.D., a YUHCHAU CHEN, Ph.D., M.D., a ALAN W. KATZ, M.D., M.P.H., a ANN G. MIHIS, B.S., a ABRAHAM PHILP, C.M.D., a PAUL OKUNIEFF, M.D., a and MICHAEL T. MILANO, M.D., Ph.D. a

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IJROBP, 2009

Review of randomized clinical trials in brain metastases
Open issues

1) Do patients with limited metastases really benefit from local treatments (including SBRT)?

2) Is it possible to identify particular pts subsets which can benefit more from local treatments (role of host-related factors underlying the oligometastatic state, i.e. miRNA)?

3) Which is the optimal RT dose?

4) What radiobiological mechanisms are relevant in the treatment of the target tumor (i.e. SBRT as “immunomodulator” or abscopal-effect inducer)?
Some Factors in Over Treatment of Patients with Advanced Cancer

- Inexperience
- Inappropriate expectations
  - Patient
  - Physician
- Pressure from relatives/colleagues
- “Give hope”
- Inadequate communication
- Departmental policy

‘I BELIEVE THAT CURE IS RARE WHILE THE NEED FOR CARE IS WIDESPREAD AND THE PURSUIT OF CURE AT ALL COSTS MAY RESTRICT THE SUPPLY OF CARE’.

Cochrane 1971