Supportive Oncology and Palliative Radiotherapy

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I have no financial disclosures relevant to this presentation.
Objectives:

- To describe opportunities for collaboration between palliative care and radiation oncology
- To review a framework for thinking about the utilization of palliative radiotherapy for patients with advanced cancer
- To apply ASTRO guidelines for palliative radiotherapy to clinical practice
Some challenges....
Other challenges???
DYING IN AMERICA
Improving Quality and Honoring Individual Preferences Near the End of Life
What is palliative care?

Center to Advance Palliative Care (CAPC):

Palliative care is specialized medical care for people with serious illnesses. This type of care is focused on providing patients with relief from the symptoms, pain, and stress of a serious illness - whatever the diagnosis.

The goal is to improve quality of life for both the patient and the family. Palliative care is provided by a team of doctors, nurses, and other specialists who work with a patient's other doctors to provide an extra layer of support. Palliative care is appropriate at any age and at any stage in a serious illness, and can be provided together with curative treatment.

https://www.capc.org/
ASTRO Choosing Wisely Campaign #8:

“Don’t initiate non-curative radiation therapy without defining the goals of treatment with the patient and considering palliative care referral.”
Palliative Care: An Extra Layer of Support

- Improves quality of life
- Reduces symptom burden
- Reduces depression
- Increases patient and family satisfaction with care
- May improve length of survival
- May decrease burnout among other providers
Primary versus Specialist Palliative Care

- Primary palliative care is provided by all providers including oncologists (yes, radiation oncologists) and primary care clinicians.

- Specialty palliative care is provided by clinicians who have extra training in:
  - symptom management (pain, constipation, N/V, SOB, anxiety, depression)
  - communication skills

- Specialty palliative care treats the person as well as the disease.

- Multidisciplinary team includes physicians, nurses, social workers, chaplains and other allied health professionals.
Multiple randomized trials support early palliative care

- **Temel, NEJM 2010 (MGH)**
  - Metastatic NSCLC patients at diagnosis randomized to early palliative care versus standard care
  - 151 patients (101 evaluable)
  - Significant improvements in quality of life and mood, overall survival benefit (11.6 vs 8.9 months), less aggressive care at end of life

- **Zimmerman, Lancet 2014 (Princess Margaret)**
  - Lung, GI, GU, breast, GYN cancer patients randomized to early palliative care consultation and follow-up versus standard care
  - 461 patients randomized, 393 evaluable
  - Significant improvements in symptoms, quality of life, satisfaction with care, spiritual well-being

- **Bakitas, JAMA 2009, Project ENABLE II (UAB)**
  - Advanced Practice Nurse-led intervention, randomized to intervention or usual care
  - 322 patients with metastatic GI, lung, GU, or breast cancer
  - Significant improvements in mood, quality of life, not symptoms, hospital days or ICU days compared with usual care

- **Bakitas, JCO 2015, Project ENABLE III (UAB)**
  - Randomized nurse-led intervention of early versus delayed palliative care, similar intervention to ENABLE II
  - 207 patients randomized to early versus delayed intervention (3 months later)
  - No differences in symptoms, QOL, hospital days, ICU days, but statistically significant improvement in 1-year survival (63% vs 48%, p= 0.38)
Models of Palliative Care: Current Model

Disease-Directed Therapies

Diagnosis  Palliative Care  Death and Bereavement
Models of integration of PC/Rad Onc

Models developed from clinics established in Canada:
- Rapid Access Palliative Radiotherapy Programs

Multiple models now exist in the US:
- Supportive and Palliative Radiation Oncology (SPRO) – DFCC/BWH
- Palliative Radiation Oncology Consult Service (PROC) – Mt Sinai
- CARE Track supportive oncology tumor board – UVA
- Palliative Radiation Oncology Service - Penn
**SPRO team**

- Weekly participation in palliative care interdisciplinary team meetings
- Joint patient visits with oncology and palliative care common
- Bi-weekly participation in supportive oncology tumor board
- Bi-directional education: radiation oncologist education about palliative care and palliative care education about radiation oncology
## Outcomes of integration of PC/Rad Onc

<table>
<thead>
<tr>
<th>Mt Sinai: PROC</th>
<th>DFCC/BWH: SPRO</th>
<th>UVA: CARE track/STAT RT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypofx RT (5 or fewer fx) increased 26% vs 61% for bone mets</td>
<td>Hypofx RT (5 or fewer fx) increased 22.3 to 53.5%</td>
<td>STAT-RT: Rapid turnaround highly conformal radiotherapy</td>
</tr>
<tr>
<td>More completed RT courses, similar pain relief</td>
<td>Total number of courses of pall RT for bone mets increased (~17/mo to ~25/mo)</td>
<td>CARE track: decreased hospitalizations, decreased cost, increased hospice utilization</td>
</tr>
<tr>
<td>Hospital LOS shorter (18 vs 12 days)</td>
<td>Total number of fractions delivered constant</td>
<td>STAT-RT: Improved pain control (80-90%) vs historical averages</td>
</tr>
<tr>
<td>Higher rate of referral to palliative care within 1 month</td>
<td>Integrated collaboration with palliative care</td>
<td>Integrated collaboration with palliative care</td>
</tr>
</tbody>
</table>

- Improved illness understanding?
- Less radiation at end of life?
- Earlier goals of care conversations?
- Improved symptom management?
- Radiation tailored to patient?
The question is not:

What can I offer the patient?

The question IS:

What is best for this patient at this time?
Prognostication: A complex and changing science

The surprise question:

Would you be surprised if this patient died in the next one year?

How about 6 months?

How about 30 days?

Utility of advanced RT techniques in last 6 months?
Utility of RT in last 30 days?
What might prognosis affect?

- Treatments suggested/offered by doctors
- Decisions made by patients/families
  - Medical
  - Life
- Other
  - Insurance/medical care provision
Setting the stage...

Ask explicitly:

“How much would you like to know about prognosis?”
Okay to normalize range of expectations and that not everyone wants details…

If patient wants to know, explore in more detail:

“What kind of information can I provide to you?”
Examples: statistics, best and worst case scenarios, specific event patient is hoping to live for, etc.

If patient does not want to know, will it impact decision-making? If so, explore reasons patient does not want to know.
Goals of care conversations

- The “Surprise Question”

- Starts early: begins at diagnosis, moves through disease process

- More than what residents often describe: not just “get the DNR”

- Ongoing conversation over the course of the illness trajectory: What is important to patient and family in current illness context?

- Helpful to have different team members to discuss goals: Reliance on oncology team to discuss “treatment options” may make it harder for oncology team to review goals
Why is this conversation different?

Atul Gawande, NYT, October 5, 2014
“The Best Possible Day” (from Being Mortal)

- What is (your) understanding of (your) health or condition?
- What are (your) goals if (your) health worsens?
- What are (your) fears?
- What are the trade-offs (you) are willing to make and not willing to make?
Palliative Radiotherapy

A TAILORED APPROACH TO PALLIATIVE RADIOTHERAPY

Bleeding and other symptoms
Advanced disease in the lung
Bone metastases
Brain metastases
Radiotherapy and hospice
Approach to Palliative Radiotherapy
“In a “curable” situation, radiation therapy is radical treatment and a modest complication rate is licensed. In the event of failure, palliation often is a begrudgingly accepted bonus. Such unscheduled palliation is not the issue here. When the initial objective of radiation therapy is palliation, new ground rules must be applied. Possible serious complications or even slowly self-limiting side effects of treatment are no longer acceptable. Overall treatment time must be short. Cost must be minimized. Convenience of treatment must be considered.”

- JAMA, 1964
Questions fundamental to palliative RT

♦ The most important question:

To treat or not to treat?
(based on ongoing discussions about goals, priorities, prognosis…)

♦ Other questions if treatment is appropriate:

What dose/fractionation scheme should be utilized?
What technique should be utilized?
Goals of palliative radiotherapy are constant:
- Rapid and durable symptom relief
- Minimize side effects
- Minimize treatment time

Dichotomy of palliative radiation therapy
- Tumor effect (and possibly durability) is related to dose
- Palliative effect not closely tied to dose

Thus an important question arises:
Is local tumor control important for palliation for any given patient?
Signs versus Symptom-based palliative RT

- Concept developed by van Oorschot and colleagues
- Principle is to tailor palliative radiotherapy to patient based on signs and symptoms of progressive cancer

Palliation of “symptoms” of progression
Aims may be:
• No overall effect on disease
• Alleviation of symptoms/distress
• Neither hastening nor postponing death
• Side effects unacceptable

Consider single (or few fractions)
Consider 2D/3D treatment

Palliation of “signs” of progression
Aims may be:
• Local control
• Prevention of symptoms
• Prolongation of life
• Some side effects tolerated

Consider higher BED
Consider more conformal treatment

Van Oorschot, Seminars Oncology. 2011.
Palliative Radiotherapy

A TAILORED APPROACH TO PALLIATIVE RADIOTHERAPY

**Bleeding and other symptoms**
- Advanced disease in the lung
- Bone metastases
- Brain metastases
- Radiotherapy and hospice
- Approach to Palliative Radiotherapy
Bleeding

- Complex management problem
- Alternative treatments might include:
  - Systemic therapy
  - Surgery
  - Embolization or other interventional radiology procedure
  - Active wound management and wound care

- The role of radiotherapy has been explored by site, are there generalities for management of bleeding from sites of primary or metastatic cancer?
  - A case study…
Bleeding: case study

- 72 year old woman, living independently, ignored breast mass for 10-12 years
  - Admitted 11/13 with Hgb 4.9 with fungating, bleeding breast mass
  - R arm weakness from nodal involvement of brachial plexus (apparent on exam and imaging)
  - CT C/A/P revealed diffuse bone metastases, no liver or lung metastases
  - MRI brain (for confusion) revealed dural based lesion infiltrating cortex, other dural enhancement
  - Biopsy revealed ER+ (100%) /PR+ (5%), Her2-, infiltrating adenocarcinoma into adipose tissue
  - Prognosis? Treatment recommendations?
Bleeding: Tailoring palliative RT

Presentation: 11.7.13
After 1000 cGy: 11.13.13
After 1800 cGy: 11.18.13
Tailoring radiotherapy for bleeding tumors

- Palliative radiotherapy can be highly effective in decreasing or stopping bleeding from malignant skin wounds, malignancy in head and neck, lung, and throughout the GI tract
  - Generally only effective in stopping “oozing” rather than arterial bleeding
  - Can be accomplished quite quickly, may be able to palliate with single fraction

- Appropriate dose-fractionation?
  - In progress systematic review: Higher BED -> more durable hemostasis
  - Prognosis-driven approach?
  - From curative regimens to single fraction to QUAD shot to 30 Gy in 10 fractions
Palliative Radiotherapy

A TAILORED APPROACH TO PALLIATIVE RADIOTHERAPY

- Bleeding and other symptoms
- Advanced disease in the lung
- Bone metastases
- Brain metastases
- Radiotherapy and hospice
- Approach to Palliative Radiotherapy
Palliative RT to lung: Prognosis driven approach

- ASTRO Guidelines, Palliative RT for advanced disease in the lung
    - Short course and long-course XRT produce equivalent symptom control
    - Modest survival benefit to longer dose-fractionation (30 Gy/10fx) for select patients
    - Minimal role for endobronchial brachytherapy or concurrent chemoRT

- Utilizing prognostic models from this talk (and other prognostic models), it is possible to consider different dose-fractionation schemes for patients with advanced cancer

<table>
<thead>
<tr>
<th>PROGNOSIS/CLINICAL CIRCUMSTANCE</th>
<th>TREATMENT OPTIONS</th>
</tr>
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</table>
| Prognosis < 1 mo                | • Supportive care alone
|                                 | • Short-course radiotherapy (ie, single 8-Gy fraction or 17 Gy in 2 fractions given one wk apart) |
| Prognosis > 1 mo                | • Supportive care alone
|                                 | • Short-course radiotherapy (ie, single 8-Gy fraction or 17 Gy in 2 fractions given one wk apart)
|                                 | • Higher-dose radiotherapy (≥ 30 Gy in 10 fractions) with the goal of moderately increased survival at the cost of more acute side effects |
| Locally recurrent disease       | • Supportive care alone
|                                 | • Retreatment with external beam therapy, taking into account increased acute and long-term side effect risks due to cumulative dosing
|                                 | • Brachytherapy for intraluminal obstruction by tumor |

Potential adjuvant treatments include:
- Endobronchial stenting for obstructing lesions
- Chemotherapy given in sequential rather than concurrent time frame
- Narcotic analgesics to minimize the sense of air hunger or shortness of breath

Palliative Radiotherapy

A TAILORED APPROACH TO PALLIATIVE RADIOTHERAPY

Bleeding and other symptoms
Advanced disease in the lung

**Bone metastases**

Brain metastases
Radiotherapy and hospice
Approach to Palliative Radiotherapy
ASTRO guidelines for palliative XRT


- Single fx and multi-fx equivalent for uncomplicated bone metastases
- Single fx does not produce unacceptable rates of long-term toxicity
- Surgery, vertebral augmentation do not obviate need for radiotherapy
- Advanced techniques should be reserved for clinical trials
- Update pending
Palliative XRT for bone mets is effective

- Systematic Review by Chow 2007, update 2012
  - Complete response rate 23% vs 24% (single vs multi fraction)
  - Overall response rate 58% vs 59% (single vs multi fraction)
  - Stabilization of pain upward of ~80%
  - No significant differences in acute toxicity (some studies show worse acute toxicity with multi fraction)
  - Trends toward increased risk of pathological fracture and cord compression with fewer fractions, overall low numbers
  - 2.5x more retreatment in single fraction arm (generally decided by treating physician), 20% vs 8%

ASTRO Choosing Wisely Campaign #3:
“Don’t routinely use extended fractionation schemes (>10 fractions) for palliation of bone metastases.”

AAHPM Choosing Wisely campaign #4:
“Don’t recommend more than a single fraction of palliative radiation for an uncomplicated painful bone metastasis.”
Single fraction XRT remains underutilized

- **Bekelman et al. JAMA 2013**
  - SEER-Medicare patients with prostate cancer 2006 to 2009
  - 3.8% of patients without prior complicating events received single fraction XRT to bone

- **Rutter, et al. IJROBP 2015**
  - 9,000 patients in National Cancer Data Base treated with XRT to non-spine bone mets from prostate, breast, lung cancer
  - 4.7% received 8 Gy in one fraction, 95.3% received multi-fraction
  - Increased from 3.4% in 2007 to 7.5% in 2011
What about complicated bone metastases?

- Generally use longer dose/fractionation schemes

- Little data: Pathologic fracture
  - More bone remineralization after longer dose/fractionation
  - ?dose fractionation for post-op – no randomized data

- Reirradiation
  - Normal tissue tolerance
  - Chow 2014 Lancet Oncology: reirradiation well-tolerated and effective
  - Stereotactic RT?
What about patients with short life expectancy?

- Multiple sub-group analyses of large clinical trials demonstrate that palliative radiotherapy can be beneficial (up to 50% response rates) in patients living less than 12 weeks and even in patients living less than 4 weeks.

What about spinal cord compression?

- More complicated: local control clearly matters
- Treatment informed by overall clinical trajectory, prognosis, histology, symptoms, patient goals/preferences
  - Consider using longer dose-fractionation schemes

- Phase III data: Surgery + RT better than RT alone
  - Patchell et al., Lancet 2005
  - Improved functional outcomes (ability to walk and length of duration of ability to walk) with surgery +RT vs RT alone (though RT arm underperformed)

- Phase III data: Single fraction as effective as multi-fraction in patients with poor prognosis (<3 mo) (Marranzano. Radiother Oncol. 2009. Thiriot, ASTRO abstract 2014)

- Prospective and retrospective data from Rades and colleagues and help to guide treatment decisions (see next slide) based on prognosis and outcomes from single versus multi-fraction regimens
Table 1. Significant Prognostic Factors and Corresponding Scores

<table>
<thead>
<tr>
<th>Prognostic Factor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of primary tumor</td>
<td></td>
</tr>
<tr>
<td>Breast cancer</td>
<td>8</td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>7</td>
</tr>
<tr>
<td>Myeloma/lymphoma</td>
<td>9</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>3</td>
</tr>
<tr>
<td>Other tumors</td>
<td>4</td>
</tr>
<tr>
<td>Other bone metastases at the time of RT</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>5</td>
</tr>
<tr>
<td>No</td>
<td>7</td>
</tr>
<tr>
<td>Visceral metastases at the time of RT</td>
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<tr>
<td>Yes</td>
<td>2</td>
</tr>
<tr>
<td>No</td>
<td>8</td>
</tr>
<tr>
<td>Interval from tumor diagnosis to MSCC, mo</td>
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</tr>
<tr>
<td>≤15</td>
<td>4</td>
</tr>
<tr>
<td>&gt;15</td>
<td>7</td>
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<tr>
<td>Ambulatory status before RT</td>
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<tr>
<td>Ambulatory</td>
<td>7</td>
</tr>
<tr>
<td>Nonambulatory</td>
<td>3</td>
</tr>
<tr>
<td>Time of developing motor deficits before RT, d</td>
<td></td>
</tr>
<tr>
<td>1-7</td>
<td>3</td>
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<tr>
<td>8-14</td>
<td>6</td>
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<tr>
<td>&gt;14</td>
<td>8</td>
</tr>
</tbody>
</table>

RT indicates radiotherapy; MSCC, metastatic spinal cord compression.

Figure 2. Kaplan-Meier curves of the 3 newly designed groups of patients (Pts) in the current study are shown with respect to survival (Group I: 20-30 points; Group II: 31-35 points; and Group III: 36-45 points).
What about SBRT for bone mets?

- No completed RCTs compare conformal radiotherapy to stereotactic radiotherapy for bone mets

- **Prospective and retrospective single institution series**
  - Novel endpoints: local control
  - Improved pain relief
  - Higher cost

- **Potential utility**
  - Spine metastases
  - Oligometastatic disease
  - Reirradiation

- **ASTRO guidelines for bone mets (2011)**
  - Not for cord compression
  - Use in clinical trials

- **Cost effectiveness analysis, Rutter, IJROBP 2015**
  - Assuming 20% improvement in pain control: survival needs to be >11 months for QALY <$100,000
Palliative Radiotherapy

A TAILORED APPROACH TO PALLIATIVE RADIOTHERAPY

Bleeding and other symptoms
Advanced disease in the lung
Bone metastases

Brain metastases
Radiotherapy and hospice
Approach to Palliative Radiotherapy
Multiple treatment modalities effective for brain metastases

- **ASTRO consensus guidelines (2012)**
  - Reviews evidence for surgery, stereotactic radiotherapy, whole brain radiotherapy, “best supportive care”

- **Multiple factors impact combinations of the various treatment approaches**
  - Data from randomized controlled trials
    - Survival
    - Brain control
    - Neurocognitive outcomes
  - Number of brain metastases
  - Prognosis
  - Patient preference

Tsao, PRO, 2012.
### Diagnosis-Specific Graded Prognostic Assessment

#### Non-small-cell and small-cell lung cancer

<table>
<thead>
<tr>
<th>Prognostic Factor</th>
<th>GPA Scoring Criteria</th>
<th>Patient Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>&gt; 60</td>
<td>≥ 60</td>
</tr>
<tr>
<td></td>
<td>50-60</td>
<td>50</td>
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<tr>
<td></td>
<td>&lt; 50</td>
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<tr>
<td>KPS</td>
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<td>≤ 70</td>
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<tr>
<td></td>
<td>70-80</td>
<td>70-80</td>
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<td>90-100</td>
<td>90-100</td>
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<tr>
<td>ECO</td>
<td>Present</td>
<td>Present</td>
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<tr>
<td></td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>No. of BM</td>
<td>&gt; 3</td>
<td>≥ 3</td>
</tr>
<tr>
<td></td>
<td>2-3</td>
<td>2-3</td>
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<tr>
<td>Sum total</td>
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</table>

Median survival (months) by GPA: 0-1.0 = 3.0; 1.5-2.0 = 5.5; 2.5-3.0 = 9.4; 3.5-4.0 = 14.8

#### Melanoma

<table>
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<tr>
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<tr>
<td>No. of BM</td>
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<td>2-3</td>
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<tr>
<td>Sum total</td>
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</table>

Median survival (months) by GPA: 0-1.0 = 3.4; 1.5-2.0 = 4.7; 2.5-3.0 = 8.8; 3.5-4.0 = 13.2

#### Breast cancer

<table>
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<th>Patient Score</th>
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<tr>
<td>KPS</td>
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Median survival (months) by GPA: 0-1.0 = 3.4; 1.5-2.0 = 7.7; 2.5-3.0 = 15.1; 3.5-4.0 = 25.3

#### Renal cell carcinoma

<table>
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Median survival (months) by GPA: 0-1.0 = 3.3; 1.5-2.0 = 7.3; 2.5-3.0 = 11.3; 3.5-4.0 = 14.8

#### GI cancers

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<td>Sum total</td>
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</table>

Median survival (months) by GPA: 0-1.0 = 3.1; 2.0 = 4.4; 3.0 = 6.9; 4.0 = 13.5
Diagnosis-Specific Graded Prognostic Assessment

Fig 2: Kaplan-Meier curves for survival for six diagnoses by Graded Prognostic Assessment (GPA) group, demonstrating excellent separation between groups ($P < .0001$ for each diagnosis: (A) breast cancer; (B) non-small-cell lung cancer; (C) small-cell lung cancer; (D) melanoma; (E) renal cell carcinoma; and (F) GI cancer. BM, brain metastases.

Multiple randomized studies comparing local therapy (surgery and/or stereotactic radiotherapy) with and without whole brain radiotherapy as well as whole brain radiotherapy with or without local therapy

- Local therapy may improve overall survival for select patients
- Whole brain radiotherapy may improve control in rest of brain but with significant neurocognitive side effects
- Trend is toward more stereotactic radiosurgery when possible
- Next two slides are from ASTRO Brain Metastases Guidelines
## ASTRO: Management of Single Brain Metastasis

### Table 1: Single brain metastasis—initial management

<table>
<thead>
<tr>
<th>Prognostic Feature</th>
<th>Other Features</th>
<th>Treatment Options (Evidence Grade)</th>
<th>Clinical Benefit</th>
</tr>
</thead>
</table>
| **Good Prognosis** | Complete Resection Possible | If brain metastasis ≤3-4 cm:  
- Surgery and WBRT (level 1)  
- Radiosurgery and WBRT (level 1)  
- Radiosurgery alone (Level 1)  | ✓ ✓ ✓ |
| **Expected Survival 3 mo or more** |  | If brain metastasis >3-4 cm:  
- Surgery and WBRT (level 1)  
- Radiosurgery with radiosurgery/radiation boost to the resection cavity with or without WBRT (level 3)  | ✓ ✓ ✓ |
| **Good Prognosis** | Not Resectable | If brain metastasis ≤3-4 cm:  
- Radiosurgery and WBRT (level 1)  
- Radiosurgery alone (level 1)  | ✓ ✓ ✓ |
| **Expected Survival 3 mo or more** |  | If brain metastasis >3-4 cm:  
- WBRT (level 3), with consideration of biopsy, if primary unknown | ✓ ✓ ✓ |
| **Poor Prognosis** |  | WBRT (level 3)  
- Palliative care without WBRT (level 3)  | ✓ ✓ |

KPS, Karnofsky performance status; LC, local control; S, survival; WB, whole brain; WBRT, whole brain radiotherapy.

Surgery may be favored if the diagnosis is uncertain (e.g., no known primary cancer or remote history of cancer and no known extracranial metastases or metastasis).

- Prognostic category based on known prognostic factors (see clinical question 1, references 13-21).
- Excluding radiosensitive histologies (e.g., small cell lung cancer, leukemia, lymphoma, germ cell tumor). A 6%-9% minority of patients in Radiation Therapy Oncology Group (RTOG) 9508 trial had small cell lung cancer.
### Table 2: Multiple brain metastases-initial management

<table>
<thead>
<tr>
<th>Prognostic category (a)</th>
<th>Other features</th>
<th>Treatment options (evidence grade) references</th>
<th>Clinical benefit</th>
</tr>
</thead>
</table>
| **Good prognosis**     | All brain metastases ≤3-4 cmb | • Radiosurgery and WBRT (level 1)\(^{51,53}\)  
• Radiosurgery alone\(^{25,54}\) (level 1)  
• WBRT (level 1)\(^{59,85}\) | ✓  
•  
• |
| **Expected survival 3 mo or more** | Brain metastasis/metastases causing significant mass effectc | • Safe surgical resection of the brain metastasis/metastases causing significant mass effect and postoperative WBRT (level 3)\(^{25,\text{b}}\)  
• WBRT (level 3)\(^{59,85}\) | ✓  
•  
• |
| **Poor prognosis**     | WBRT (level 3)\(^{59,85}\)  
• Palliative care without WBRT (level 3)\(^{59,85}\) | ✓  
•  
• |

KPS, Karnofsky performance status; LC, local control; S, survival; WB, whole brain; WBRT, whole brain radiotherapy. Surgery may be favored if the diagnosis is uncertain (eg, no known primary cancer or remote history of cancer and no known extracranial metastases or metastasis).

- **Prognostic category based on known prognostic factors (see clinical question 1, references 13-21).**
- **Excluding radiosensitive histologies (eg, small cell lung cancer, leukemia, lymphoma, germ cell tumor). A 6%-9% minority of patients in RTOG 9508 trial had small cell lung cancer.**
- **The maximum number or total volume of brain metastases best treated with radiosurgery (or surgery) is unknown. Randomized trials which have examined the use of radiosurgery, included selected patients with up to 4 brain metastases, while retrospective reports document use of radiosurgery that exceed 4 brain metastases.\(^{52,55}\) A retrospective study\(^{25}\) suggested that surgery significantly improves survival if all brain metastases can be removed.**
Recurrent or Progressive Brain Metastases

- Case-by-case basis. Factor in status of extracranial disease, performance status, co-morbidities, patient wishes, and prognosis
- Repeat WBRT in select patients with better than 3-6 months after initial WBRT. Median survival after re-irradiation was 2.5-5.2 months with up to 68% of patients (Son 2012, Morris 2000)
What is the role of WBRT for poor prognosis patients?

- **QUARTZ trial**: MRC randomized trial evaluating quality of life after whole brain XRT for patients with inoperable brain metastases from NSCLC
  - Randomized to Optimal Supportive Care versus Optimal Supportive Care + WBRT 400 cGy x 5 fractions
  - Primary endpoint is quality adjusted life years

- **Final results reported ASCO 2015**
  - No difference between patients who received WBRT and OSC versus OSC alone with regard to overall survival, quality adjusted life years or quality of life

- **Fundamental questions remain**
  - What is the role of whole brain radiation for patients with poor prognosis? Many brain metastases? Leptomeningeal disease?
  - It is ALL in the discussion…
Palliative Radiotherapy

A TAILORED APPROACH TO PALLIATIVE RADIOTHERAPY

- Bleeding and other symptoms
- Advanced disease in the lung
- Bone metastases
- Brain metastases

Radiotherapy and hospice

Approach to Palliative Radiotherapy
Palliative XRT in last 30 days of life is often multi-fraction

**SEER-Medicare study (2013)**

- Evaluated use and cost of XRT among 200,000 patients who died from lung, breast, prostate, colorectal, pancreatic cancer 2001-2007 (not all necessarily palliative)
- 7.6% of patients received XRT in last 30 days of life
- Of those, 17.8% received >10 days of treatment
- Radiation site not determined

- Radiotherapy use in last 30 days of life decreased from 2001-2007

- Hospice enrollment associated with decreased # of fractions and decreased total cost
Palliative XRT and hospice

♦ SEER-Medicare study (2014)
  • Evaluated use and cost of XRT among 7,000 patients who completed palliative XRT within 30 days of hospice enrollment
  • Median Length of XRT: 14 days
  • Median Length of Hospice Enrollment: 13 days
  • Radiation site not determined

A

B

Yeung H. JPSM. 2014.
# Barriers to palliative RT use in hospice

## ASTRO and NHPCO survey 2002

<table>
<thead>
<tr>
<th>What are the barriers?</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 76% feel radiation oncologists resist single fx</td>
</tr>
<tr>
<td>• Treatment length too long</td>
</tr>
<tr>
<td>• Radiation oncology expense</td>
</tr>
<tr>
<td>• Travel concerns</td>
</tr>
<tr>
<td>• Concerns about life expectancy – is it worth it?</td>
</tr>
<tr>
<td>• Patient and family reluctance</td>
</tr>
<tr>
<td>• Poor communication with radiation oncologist</td>
</tr>
<tr>
<td>• Radiation is ineffective</td>
</tr>
</tbody>
</table>

## VCU survey 2011-2012

<table>
<thead>
<tr>
<th>What is the #1 barrier?</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Transportation (cost, availability)</td>
</tr>
<tr>
<td>• Number of treatments</td>
</tr>
<tr>
<td>• Access (more doctors, appts)</td>
</tr>
<tr>
<td>• Patient frailty</td>
</tr>
<tr>
<td>• Treatment early enough for benefit?</td>
</tr>
<tr>
<td>• Clinician inexperience</td>
</tr>
<tr>
<td>• False hope</td>
</tr>
<tr>
<td>• Poor communication</td>
</tr>
<tr>
<td>• Side effects</td>
</tr>
<tr>
<td>• Resistance to single fraction</td>
</tr>
</tbody>
</table>

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Schuster, JHPN, 2014.
Clinic Offering Affordable Radiation Therapy to Increase Access to Care for Patients Enrolled in Hospice

- VCU program: 18 month trial
- Designed to allow triage, consultation, simulation and treatment with single fraction all within 4 hour visit at affordable cost (flat rate $400)
- 8 patients referred
  - 2 screened out at telephone screening
  - 2 underwent CT simulation, not candidates
  - 4 received palliative single fraction palliative RT

Schuster, JOP, 2014.
Palliative Radiotherapy

A TAILORED APPROACH TO PALLIATIVE RADIOTHERAPY

- Bleeding and other symptoms
- Advanced disease in the lung
- Bone metastases
- Brain metastases
- Radiotherapy and hospice

Approach to Palliative Radiotherapy
Factors affecting dose/fractionation

<table>
<thead>
<tr>
<th>Factors suggestive of a more aggressive approach (highly conformal or stereotactic treatment, or prolonged fractionation)</th>
<th>Factors suggestive of a less aggressive approach (less conformal treatment, short fractionation)</th>
<th>Factors suggestive of palliative care without radiotherapy intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prognosis likely &gt;6 months (see accompanying text)</td>
<td>Prognosis likely 1-6 months</td>
<td>Prognosis likely &lt;1 month</td>
</tr>
<tr>
<td>Good performance status (KPS ≥70)</td>
<td>Poor performance status (KPS &lt;70)</td>
<td>Very poor performance status/death imminent</td>
</tr>
<tr>
<td>Systemic disease well controlled</td>
<td>Large burden of systemic disease</td>
<td>Overwhelming burden of symptoms—radiotherapy affecting one symptom among many</td>
</tr>
<tr>
<td>Effective systemic treatments available*</td>
<td>Few or no proven effective systemic treatments available*</td>
<td>No effective systemic treatments available*</td>
</tr>
<tr>
<td>Large symptomatic tumor (less likely to respond to lower doses of radiotherapy)</td>
<td>Small symptomatic tumor (more likely to respond to lower doses of radiotherapy)</td>
<td></td>
</tr>
<tr>
<td>High likelihood of significant late side effects due to normal tissue exposure</td>
<td>Low likelihood of significant late side effects</td>
<td>High likelihood of acute side effects that the patient may not survive</td>
</tr>
<tr>
<td>High morbidity of possible recurrence</td>
<td>Low morbidity of possible recurrence</td>
<td></td>
</tr>
<tr>
<td>High morbidity of retreatment</td>
<td>Low morbidity of retreatment</td>
<td>Retreatment in an area that would exceed critical normal tissue tolerance</td>
</tr>
<tr>
<td>Few or no effective alternative palliative therapies</td>
<td>Range of effective alternative palliative therapies</td>
<td>If radiotherapy prohibits other effective palliative therapies (i.e., delay of referral to hospice)</td>
</tr>
</tbody>
</table>

* Effective systemic treatments may be based on the histology and biology of the primary cancer (i.e., metastatic hormone receptor positive metastatic breast cancer versus metastatic squamous cell carcinoma of the lung) and number and effect of prior treatment regimens; ** Psychosocial issues (such as transportation issues, wanting to live to experience a specific event, wanting to spend time with family, etc.) that emerge in conversations with patients and family may cross categories in either direction.
<table>
<thead>
<tr>
<th>Site</th>
<th>Common Sx</th>
<th>Poor prognosis</th>
<th>Avg. prognosis</th>
</tr>
</thead>
</table>
| CNS        | • Headache  
             • Neurologic deficits | • 30-40 Gy in 10-15 fx  
             • Supportive care alone | • 59-60 Gy in 30-35 fx  
             • Supportive care alone |
| Head & Neck| • Pain  
             • Bleeding  
             • Airway compromise | • 14 Gy in 4 fx/mo to 42 Gy  
             • 8 Gy x 1-3 fx  
             • Supportive care alone | • 70 Gy in 35 fx  
             • Altered fractionation  
             • ChemoRT |
| Breast     | • Pain  
             • Ulceration/bleeding  
             • Plexopathy | • 20-30 Gy in 4-5 fx  
             • 8-10 Gy in 1 fx  
             • Supportive care alone | • 30 Gy in 10 fx  
             • 50 Gy in 20 fx  
             • 42-66 Gy in 16-33fx |
| Lung       | • Pain  
             • Dyspnea/cough  
             • Hemoptysis | • 17 Gy in 2 fx in 2 wks  
             • 8-10 Gy in 1 fx  
             • Supportive care alone | • > BED of 30 Gy/10 fx  
             • Endobronch brachy for obstruction |
| Esophagus  | • Dysphagia  
             • Bleeding  
             • Obstruction | • 30 Gy in 10 fx  
             • 8-24 Gy in 1-3 fx  
             • Supportive care alone | • 50 Gy in 25 fx  
             • 50 Gy in 20 fx |
| GU/GYN     | • Pain  
             • Bleeding  
             • Obstruction | • 14.4 Gy in 4 fx/mo to 43.2 Gy  
             • 8-10 Gy in 1 fx  
             • Supportive care alone | • 30 Gy in 10 fx  
             • 50 Gy in 20 fx |
| Lymphoma   | • Varied based on site | • 4-8 Gy in 2 fractions  
             • Supportive care alone | • 20-40 Gy in 10-20 fx  
             • Supportive care alone |

Adapted from Lutz, S, JCO, 2014.
Future Directions

♦ **SPRO: Society for Palliative Radiation Oncology**
  - Formed 2014, international collaboration including members from ASTRO, CARO, ESTRO, RANCZR
  - Three subgroups:
    - Education
    - Research
    - Advocacy
  - Overall leadership under Steve Lutz, MD

♦ **Palliative Oncology Symposium**
  - Joint venture of ASTRO, ASCO, AAHPM, MASCC
  - Next conference 9/16 in San Francisco; abstract submission deadline in May
  - Plan for annual meeting on education and research into integrating palliative care in oncology
## Future opportunities for collaboration

<table>
<thead>
<tr>
<th>Factor</th>
<th>Initiative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Residency training</td>
<td>Formalized role of palliative care training in radiation oncology residency</td>
</tr>
<tr>
<td>Board certification</td>
<td>Expanded role of radiotherapy in hospice and palliative medicine boards</td>
</tr>
<tr>
<td>Clinical teams</td>
<td>Dedicated academic palliative radiotherapy services</td>
</tr>
<tr>
<td>Referral patterns</td>
<td>Early palliative care referral for appropriate radiotherapy patients</td>
</tr>
<tr>
<td>Course length</td>
<td>More hypofractionated courses for end-of-life radiotherapy patients</td>
</tr>
<tr>
<td>Prognosis</td>
<td>Further development and use of accurate prognostic instrument</td>
</tr>
<tr>
<td>Overuse measures</td>
<td>Formation of more radiotherapy overuse guidelines and quality measures</td>
</tr>
</tbody>
</table>

Conclusions

- Palliative care is a medical specialty that can provide assistance with symptom management and complex communication tasks for patients with advanced illness.
- Early palliative care for patients with incurable cancer has been shown to improve quality of life and survival; integration with radiation oncology may further improve outcomes.
- Palliative radiotherapy is a safe, effective treatment for various symptoms of advanced cancer.
- A prognosis driven approach to palliative radiotherapy can tailor dose-fractionation to individual patients.
- Guidelines for palliative radiotherapy can help to tailor radiotherapy appropriately for individual patients.
Questions?

- Thank you for your attention.
- Contact information:
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