Radiation for Palliation

John M. Holland, MD
OHSU Radiation Oncology
September 1, 2010
Radiation for Palliation

- First, the Good News
- There is No Quiz!!!

- Now, the Bad News
- There is a Lecture!!
Radiation for Palliation

- And even worse news....
- I lied
- There is A QUIZ!!!
Radiation for Palliation

1) Brain Metastases
2) Superior Vena Cava Syndrome
3) Airway Symptoms: obstruction/hemoptysis
4) Dysphagia
5) GYN/GI Cancer Symptoms
6) Hepatic Metastases
7) Bone Metastases
8) Spinal Cord Compression
Radiation for Brain Metastases: Background

- Brain metastases develop in 10-30% of adults with cancer and 6-10% of children with cancer.
- In the US, this results in 97,000-170,000 new cases of patients with brain metastases per year.
- This may be increasing with greater use of MRI leading to greater diagnosis and improved chemotherapy leading to prolonged survival.
- Most common primaries are: lung (50%), breast (15-20%), unknown primary (10-15%), melanoma (10%), colorectal (5%).
- One-third to one-fourth of patients will present with solitary metastasis; breast, colon and renal tumors are often solitary, lung and melanoma often present with diffuse disease.
Radiation for Brain Metastases: Presenting Symptoms

- About two-thirds of patients with brain metastases will develop neurologic symptoms.
- Most patients present with progressive dysfunction due to expanding tumor or edema around the tumor.
- 40-50% will have headaches.
- One-third will present with cognitive dysfunction (memory loss, mood/personality changes).
- Focal neurologic signs (weakness) are seen in 20-40%.
- About 10-20% will present with seizures; about 5-10% will present with strokes due to tumor emboli or hemorrhagic brain mets (melanoma, renal cell, choriocarcinoma and thyroid tumors often bleed).
Radiation for Brain Metastases: Medical Treatment

- Steroids are important to decrease edema.
- Steroids produce anti-edema effect by decreasing tumor capillary permeability.
- Load with 10-20 mg then follow with 4 mg QID.
- Anticonvulsants are necessary only for patients who present with seizures.
Brain Metastases: Surgery

- Patients with or without active systemic disease were randomized to receive:
  1) whole brain RT (WBRT) alone (36 Gy/12 fxs)
  2) Resection followed by WBRT
- Patients having surgery had fewer intracranial recurrences: 20% vs. 52% and **improved survival: 40 weeks vs. 15 weeks**.
Brain Metastases: Patchell
Overall Survival
Brain Metastases: Patchell’s Second Study

- Patchell next asked the value of whole brain RT after resection of solitary mets (JAMA V280, p1485-1489, 1998).
- Patients randomized to:
  1) resection alone vs.
  2) resection + WBRT (50.4 Gy/28 fxs)
- Intracranial failure rate was less after WBRT (18% vs. 70%) and patients receiving WBRT “less likely to die of neurologic causes” but overall length of survival/length of time “patients remained functionally independent” not different.
Whole Brain Radiation for Multiple Mets

- Radiation for brain metastases is **palliative** for many neurologic symptoms.
- Median survival is only increased from 3 to 6 months—many patients die from extracranial progression.
- Overall symptom response rate is 64-85%.
- Cairncross reported 74% improvement of neurologic symptoms (such as headache) with 65% improved for at least 9 months or duration of life (*Ann Neurol* V7, p529-541, 1980).
- Cranial nerve dysfunction improves in 40% (most effective when RT is delivered **early**).
Whole Brain Radiation for Multiple Mets: Optimal Dose-Fractionation

- RTOG has conducted trials evaluating dose-fractionation in patients with brain metastases.
- Dose-fractionation schedules ranging from 40 Gy in 4 weeks to 20 Gy in one week have been compared (Oncolgy V9, p 1205-1211, 1995).
- Median survival ranges from 15 to 18 weeks with brain metastases being the cause of death in 40%.
- Symptoms were palliated in 75-80%.
- Short schedules with large fractions resulted in quickest but least durable palliation.
Whole Brain Radiation for Multiple Mets: Ultrarapid Fractionation

- Ultrarapid fractionation has been studied by RTOG with 10 Gy x 1 or 12 Gy in 2 fractions (IJROBP V 7 p 1633-1638, 1981).
- Neurologic improvement and survival rates were similar to more protracted courses of RT but duration of improvement was shorter: 4 weeks vs. 10 weeks.
- RTOG has established 30 Gy/10 fractions as “standard treatment”.
Radiosurgery for Brain Metastases: Background

- Stereotactic radiosurgery uses highly focused, precise beams of radiation centered on a small treatment volume.
- Since precision is key, less normal tissue is radiated and **higher doses** can be delivered.
- **Immobilization** of the target is also critical.
- Radiosurgery for brain metastases generally fits these criteria with **small, immobilizable targets**.
- Radiosurgery can be delivered by a **Gamma Knife** or can be **Linac-Based**.
- The **CyberKnife** can also perform intracranial (as well as extracranial) radiosurgery.
Radiosurgery: Gamma Knife

- The Gamma Knife focuses 201 Co60 gamma radiation beams on a target.
- The sources are placed in a circular shielded unit.
- A high dose is delivered to the point of intersection but little radiation is delivered elsewhere (precise to within 0.3 mm).
- Gamma Knife is also effective against AVMs, acoustic neuromas, meningiomas.
Gamma Knife Perfexion
Radiosurgery: Gamma Knife

The Gamma Knife delivers high-intensity radiation to a brain tumor with sophisticated imaging and a head-stabilizing helmet dotted with adjustable apertures.

(Fig. 1) MRI scan at the time of Gamma Knife radiosurgery (left) showing a metastatic adenocarcinoma of the brain. Eight months after radiosurgery, an MRI scan was normal (right). Significant tumor reduction was identified six weeks after treatment.
LINAC-Based Radiosurgery

- Radiosurgery can also be delivered using a linear accelerator - the same machine used for other radiation oncology treatments.
- Like the gamma knife, this radiosurgery is non-invasive and uses convergent beams to deliver a large dose of radiation to limited single target.
- Using LINAC-based radiosurgery, the target is placed in the center of a series of narrow rotating (arc) beams of radiation.
- Usually radiosurgery is performed in a single day.
- Complications are “minor” with less than 2% risk for hemorrhage, cranial nerve damage or necrosis.
LINAC-Based Radiosurgery
CyberKnife Radiosurgery

CyberKnife: intracranial and extracranial radiosurgery
Radiosurgery for Brain Metastases

- RTOG 9508 evaluated whole brain RT +/- stereotactic boost for patients with brain metastases.
- 333 patients with 1-3 mets all received WBRT: 37.5 Gy/2.5 Gy.
- Stereotactic radiosurgery completed within week of WBRT.
- Intracranial control was superior with SRS.
- Recursive partitioning analysis class 1 (favorable patients) tended to benefit from SRS (P<0.0001)
- Patients with “favorable” histology: squamous lung cancer also did better with SRS (p=0.02)
- The addition of stereotactic radiosurgery improved “functional autonomy” as measured by KPS at 6 months.
- Patients with single brain metastasis had improved survival with addition of SRS (6.5 vs. 4.9 months, p=0.04)
Radiosurgery: Do We Need Whole Brain RT?

- The value of adding whole brain RT to SRS is controversial.
- WBRT did not improve median survival time, brain freedom from progression or freedom from new brain metastases in patients with breast cancer brain mets at UCSF (IJROBP 2009;75:1132-1140).
- WBRT resulted in improved local control patients with tumor volume $\geq 2\text{cc}$, peripheral dose $<16\text{ Gy}$, single lesions, nonradioresistant tumors, and lung cancer mets in patients surviving at least one year after Gamma Knife at Pittsburgh. Distal intracranial failure was similar at 5 years (75% vs. 62%). WBRT did not improve survival. (IJROBP 2005; 62:1125-1132)
Others have suggested that addition of WBRT may be beneficial for select patients
Patients with good prognostic features may benefit
RPA Class I (KPS≥70%, age <65, controlled primary, no extracranial mets)
RPA class I patients had better survival with WBRT + SRS vs. SRS alone in Korean study of SRS for 1-10 mets (IJROBP 2010, ahead of print)
Japanese randomized study of 132 patients with 1-4 mets, each <3 cm compared SRS alone (67 patients) vs. WBRT + SRS (JAMA 2006;295:2483-2491)
Median survival time: 7.5 months
Brain tumor recurrence rate less with WBRT (47% vs. 76%)
No difference in survival or “neurologic caused” death
Superior Vena Cava Syndrome

- Tumors can compress, obstruct or lead to thrombosis within the superior vena cava (SVC).
- This will lead to swelling of the face, neck and arms.
- Collateral circulation over the trunk may develop if onset of obstruction has been gradual.
- 95% of patients with SVC syndrome have cancer; 75% of these are lung cancers (others include lymphomas, mets, germ cell tumors)
- About 4% of all lung cancer patients will develop superior vena cava syndrome.
- Patients are often referred for urgent radiotherapy due to severe dyspnea and orthopnea.
Superior Vena Cava Syndrome
Superior Vena Cava Syndrome

- Chemotherapy is used to treat lymphomas and small cell lung carcinoma.
- Corticosteroids may provide some symptomatic relief.
- “Most effective” palliation with radiation involves initial large fraction size (3.5 Gy- 4 Gy for first 3-4 days) to quickly relieve dyspnea.
- Lymphomas/small cell carcinoma respond more quickly.
- 62-80% of small cell patients will have a good response
- Only 46% of NSCLC will achieve palliation
  - (Archives of Internal Medicine 153(3): 384-387, 1993)
Radiation to Relieve Airway Symptoms

- Hemoptysis is a frequent presenting symptom of lung cancer.
- About 30-60% of patients with lung cancer will have hemoptysis.
- When associated with cancer, the symptom usually persists for longer than one week and “large amounts of blood” (>30 ml) are produced per episode.
- Massive hemoptysis can be fatal with death due to asphyxiation.
- Hemoptysis is usually well palliated by RT: 83% response (Radiology 1979 Jul;132(1):175-6)
Radiation to Relieve Airway Symptoms

- Patients with lung cancer often present with signs/symptoms related to obstruction (dyspnea, pneumonia, etc.)
- Radiotherapy can be used to relieve obstruction.
- XRT may relieve atelectasis in only 23% overall (these results are better for small cell: 57%).
- Likelihood of relief of obstruction is related to the duration of obstruction/lung collapse.
- Reddy reported that 71% treated within 2 weeks of radiographic obstruction had complete re-expansion compared to only 23% of those treated after 2 weeks of collapse.
Radiation to Relieve Airway Symptoms

- When symptomatic disease is **limited to the airway**, **endobronchial brachytherapy** can be performed.
- Here, catheters are placed across the disease and radioactive wires/seeds are placed to deliver focal radiation.
- High-dose rate or low-dose rate radiation can be used.
- Mehta reports a **78%** rate of **symptomatic improvement** after endobronchial brachytherapy.
- **>50%** maintained life-time palliation.
- Endobronchial brachytherapy does carry risks for **hemoptysis** and **fistulae**.
Brachytherapy: Remote Afterloading with High-Dose Rate (HDR) Ir-192

Single 10 Ci Ir-192 source on cable
Endobronchial Brachytherapy

Schematic of the catheter within the airway. The tumor surrounding the catheter receives high doses of radiation via endobronchial implant within a short period of time. This treatment is associated with a high likelihood of improving shortness of breath, post-obstructive pneumonia and bleeding related to the tumor.
Radiation for Brachial Plexus Infiltration
What’s the Diagnosis?
Radiation for Palliation of Nerve Impingement Symptoms: The Chest

- Patients with superior sulcus tumors can develop Horner’s Syndrome with impingement of the sympathetic nerve chain.
- This leads to ptosis, miosis, anhydrosis and enophthalmosis.
- Even with tumor cure/control, neurologic recovery is rare.
- Pain relief from these tumors invading into the brachial plexus can be achieved with RT.
- Ampil reviewed 23 cases of carcinomatous brachial plexopathy and found “significant pain relief” in 77%.
  
  (Cancer 1985 Nov 1;56(9):2185-8)
- Hoarseness resulting from tumor damage to the recurrent laryngeal nerve (usually due to adenopathy in the AP window) is usually poorly palliated (unless from lymphoma/small cell).
Esophageal Cancer: Dysphagia

*Figure 1. Thoracic tomography. Arrow shows esophageal tumor.*
Radiation to Relieve Dysphagia from Esophagus Cancer

- Most patients with esophageal cancer will present with dysphagia - difficulty swallowing.
- Rosenberg reported that RT can be used to relieve pain and dysphagia in up to 80%. (Curr Probl Cancer. 1981 May;5(11):1-52)
- Wara reported 89% palliation rate; 66% lasting 2 months or more (Radiology 1976 Dec;121(3 Pt. 1):717-20)
- Coia reported a greater response (91%) and quicker relief from dysphagia when RT was combined with chemotherapy. (Cancer V71 p 281-286, 1993)
- Endoluminal brachytherapy can be used for dysphagia: Sharma reported 48% improvement following HDR at the risk of stricture, ulcer or fistula (IJROBP 2002 Feb;52(2):310-5)
GYN Palliation
Radiation to Palliate GYN Cancer Symptoms

- Patients with cervix cancer can present with **massive bleeding**.
- Two or three fractions of radiation (total 5-6 Gy) can be delivered to help **control bleeding** and allow staging/definitive therapy.
- Recurrent GYN tumors can present with **pain, bleeding** and **discharge**.
Radiation to Palliate GYN Cancer Symptoms

- Short-course RT can be effective in these cases.
- Onsrud reported on the use of a single 10 Gy fraction for patients requiring palliation for cervix and endometrial cancers.
- Vaginal bleeding stopped in 90%, “malodorous discharge” was relieved in 39%.
- Median survival was 9 months; 6% had “serious” GI complication from RT.
  - (Gynecol Oncol 2001 Jul;82(1):167-71)
- RTOG has also used 2 days of BID RT “the Quad Shot” (370 cGy/fx to 1480 cGy/course) Q 4-6 weeks for “advanced pelvic tumors”.
  - (IJROBP 1989 Sep;17(3):659-61)
Radiation for Sacral Plexopathy
Radiation for Palliation in Recurrent Rectal Cancer

- Patients with recurrent rectal cancer can present with bleeding, pain and obstruction.
- Often obstruction can be treated with colostomy.
- Regional recurrences are often located in the presacral space with tumor invading into the sacral plexus causing intractable pain.
- Further, many of these patients will have received radiation as part of up-front therapy before developing recurrence.
- Lingareddy reported the use of pelvic re-irradiation (median dose 30.6 Gy) for inoperable, recurrent rectal cancer.
- “Bleeding, pain, and mass effect were palliated completely in 100, 65, and 24% of instances, respectively, and the majority of responding patients were palliated until death”.
- (IJROBP 1997 Jul 1;38(4):785-90)
Pain with Unresectable Pancreas Cancer
Radiation for Painful Unresectable Pancreas Cancer

- Celiac plexopathy

- Radiation fairly effective in providing **significant** and **durable** pain relief

- Morganti: after brief RT (30 Gy) 50% needed no pain meds, 25% reduced narcotics (**75% pain response**); only 17% required later increase in pain meds (J Palliat Care V19 (2003) p. 258-262)

- Azria reports a 74% reduction in pain in patients receiving chemoRT (Pancreas V25 (2002) p. 360-5)
Radiation for Palliation of Liver Metastases

- Liver metastases are common in patients with gastrointestinal (colorectal, pancreas, stomach) cancers.
- Other cancers with frequent spread to the liver include lung, breast and melanoma.
Radiation for Palliation of Liver Metastases

- Rarely, liver metastases can become diffuse, large and **painful**.
- Leibel has reported using 21 Gy/3 Gy fxs whole liver radiation for palliation.
- 187 evaluable patients.
- **80% symptomatic improvement** after RT.
- Complete pain relief in **54%**.
- Pain relief was prompt - **median time to relief was 1.7 weeks**.
- Liver mets from **colon cancer** best palliated.
- **KPS improved in 28%**.
- ([IJROBP 1987 Jul;13(7):1057-64](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2434378/))
Radiation for Bone Metastases: Background

- Metastatic spread to bone is **common**.
- **Breast, prostate, lung** cancers account for **50-80%** of bone mets.
- Other common primaries include kidney and thyroid.
- Hematologic cancers can cause bone destruction - **lymphoma, myeloma**.
- **70%** of mets involve **axial skeleton**: cranium, ribs, spine/sacrum.
- About **75%** of patients with bone metastases will **have pain**.
Metastatic Prostate Cancer on Bone Scan: “Superscan”
Radiation for Bone Metastases: Reasons for RT

- We treat bone metastases for three reasons:
  - 1) To **relieve pain**;
  - 2) To prevent/decrease the risk of **pathologic fracture**;
  - 3) To prevent **neurologic compression**
    - a) **nerve root**
    - b) **cauda equina**
    - c) **spinal cord**

**Spinal cord compression** is a radiation oncology emergency.
Spine Metastasis: Lytic
Spine Metastasis: Blastic
Radiation Relief of Malignant Bone Pain: Mechanism

- Not entirely understood

- Radiation reduces tumor bulk by killing cancer cells – both by mitotic and apoptotic death

- Radiation kills inflammatory cells (apoptosis) decreasing release of chemical mediators/cytokines
Pain Relief through Direct Tumor Kill

- Probably **NOT** the most important pathway for pain relief

- Pain relief often **seen within 24 hours** argues against tumor shrinkage alone as reason for decreased pain


- Still even relatively low doses of RT can cause **significant tumor kill**
Radiation Pain Relief: Other Factors

- In fact, most early pain relief is due to:
  1) Reduction of cytokine release
  2) Direct damage to osteoclasts
  3) Radiation effect/damage to nerve endings
Radiation for Bone Metastases: 8 Gy x 1 vs. 3 Gy x 10 – RTOG 9714

- Multi-institution phase III trial (RTOG and NCCTG)
- Breast or prostate cancer bone metastases
- Worst pain score >5 out of 10
- Radiographic evidence of bone metastases

- Randomization: 8 Gy x 1 vs. 30 Gy in 10 fractions
- Treatment to as many as 3 painful sites.
- JNCI 2005; 97:798-804
Radiation for Bone Metastases: 8 Gy x 1 vs. 3 Gy x 10 – RTOG 9714

- 949 patients enrolled; 897 eligible for analysis
- 445 patients with prostate cancer; 452 breast

- **Higher grade 2-4 acute toxicity in 30 Gy arm:**
  - 17% vs. 10% (p=.002).
- Median survival was 9 months; 41% alive at one year, 22% at 2 years
Radiation for Bone Metastases: 8 Gy x 1 vs. 3 Gy x 10 – RTOG 9714

- Pain relief evaluated by Brief Pain Index (BPI) at 3 months
- Entire group: 17% complete response; 49% partial response (overall: 66%)
- 10% had progression of pain.
- At 3 months, 33% no longer required narcotic pain meds.
Radiation for Bone Metastases: 8 Gy x 1 vs. 3 Gy x 10 – RTOG 9714

<table>
<thead>
<tr>
<th></th>
<th>8 Gy x 1</th>
<th>3 Gy x 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete response</td>
<td>15%</td>
<td>18%</td>
</tr>
<tr>
<td>Partial Response</td>
<td>50%</td>
<td>48%</td>
</tr>
<tr>
<td>Solitary painful</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lesion CR</td>
<td>18%</td>
<td>25%</td>
</tr>
<tr>
<td>Solitary painful</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lesion PR</td>
<td>52%</td>
<td>46%</td>
</tr>
</tbody>
</table>

P=0.17
Radiation for Bone Metastases: 8 Gy x 1 vs. 3 Gy x 10 – RTOG 9714

- Pain and narcotic use relief is equivalent for both 30 Gy in 10 fractions and 8 Gy in a single fraction.
- At 3 months follow-up, there is no difference between the two treatment arms regardless of stratification.
- Subsequent pathologic fracture rate: 5% after 8 Gy x 1 vs. 4% after 3 Gy x 10
- Retreatment rate significantly higher after 8 Gy x 1: 18% vs. 9% (p<.001) – decision to retreat “left to discretion of treating physician”.
Radiation for Bone Metastases: Is 8 Gy x 1 the New Standard?

- Probably should be for most mets

- Wu recently performed review and meta-analysis and concludes: “where the treatment objective is pain relief, a single 8 Gy treatment, prescribed to the appropriate target volume, is recommended as the standard dose-fractionation schedule for the treatment of symptomatic and uncomplicated bone metastases”

- *BMC Cancer* 4 (2204) p.1-7

- Complicated bone metastases include: sites of previous RT, pathologic fractures, spinal cord/cauda equina compression
Is 8 Gy x 1 Pain relief as DURABLE?

- 8 Gy x 1 patients tend to undergo more retreatments than more protracted courses
  - Radiother Oncol V 52 (1999) p. 95-6

- This may have also been because retreatment after 8 Gy x 1 is felt to be safer retreatment by radiation oncologists

- Still, a controversial topic especially in U.S.
Radionuclide therapy with Strontium-89 (Metastron) or Samarium-153 (Quadramet) has also been used to treat patients with widespread symptomatic disease: outcomes seem best for blastic tumors like prostate or breast.

These agents are administered IV – often by nuclear medicine.
Strontium-89 (Metastron)

- As a calcium analog, strontium clears rapidly from the blood and localizes in bone
- Preferential uptake in sites of osteogenesis (blastic lesions)
- Strontium-89 is a pure beta emitter with a short range (8 mm) thereby selectively radiating bone but not surrounding soft tissues
- Dose is 4 mCi by slow IV (1-2 minutes)
- Physical half-life 50.5 days
- Maximum beta energy is 1.463 MeV
- Due to marrow effects, contraindicated if platelet count is below 60 K or WBC below 2.4 K
Samarium-153 (Quadramet)

- Samarium emits both medium energy beta particles and a gamma photon
- Because of the gamma emission, imaging can be performed after samarium injection to document uptake
- **Physical half life is short**: 46.3 hours (1.93 days)
- The average beta particle energy is 233 KeV
- With lower energy and shorter half-life, samarium marketed as having less bone marrow suppression
Radionuclide Therapy

- Single injection
- Pain relief in up to 70% (blastic lesions like breast or prostate)
- Pain relief usually occurs within a week
- Pain relief can last for months
- If blood counts are adequate, dosage can be repeated
- Can cause pain “flare”
- Not indicated when spinal cord compression

[J Clin Oncol. 1998; 16:1574-1581]
Radiation for Bone Metastases: Pathologic Fracture from Prostate Cancer
Radiation for Bone Metastases: Prevention of Pathologic Fractures

- Metastatic disease in weight bearing bones - especially the femur require RT to try to prevent pathologic fracture.
- Metastatic disease in weight bearing areas associated with greater than 50% cortical bone destruction should undergo orthopedic evaluation for surgical stabilization.
- Mirels estimates risk of pathologic fracture based upon: location, % destructed bone mass, histology, and pain.
- (Clin Orthop 1989 Dec;(249):256-64)
- After surgery, RT should be delivered covering the entire pin/rod length.
Radiation for Spinal Cord Compression

- Tumor causing spinal cord compression is a radiation oncology emergency.
- Up to 5% of pts with mets (20,000 pts/yr) suffer spinal cord compression.
- The tumor enters epidural space via contiguous spread from the adjacent vertebral body metastasis.
- First sign is usually pain.
- Pain usually will increase with a mean duration of 7 weeks from the onset of pain to the development of neurologic deficits from cord compression.
- Best results are to treat before neurologic deficit.
- MRI is best way to evaluate spine and cord.
Spinal Cord Compression
Radiation for Spinal Cord Compression

- Of 100 patients with cord compression, radiation will be completed on 60; 20 patients will progress (neurologic deterioration) during RT; 20 will not be referred due to total paralysis or imminent death. (Brain V105; p189-213, 1982).

- Most common site for cord compression is the thoracic spine.

- For patients with cord compression, the most important prognostic indicator is ability to ambulate: patients walking after treatment have median survival of 12 months; median survival is only 1 month for nonambulatory patients. (IJROBP V32; 959-967, 1995).
Radiation for Spinal Cord Compression

- Corticosteroids will help with edema around the cord; loading doses of 16-20 mg Decadron can be used followed by 4 mg Q 6 hr.

- Fully ambulatory patients may not require steroid use.
- As in other bone mets, fractionation regimen controversial.
- Most use 300 cGy x 10.

- Maranzano evaluated 255 patients receiving RT for cord compression: 71% had pain relief (54% complete, 17% partial); 76% achieved full neurologic recovery or preserved ability to walk; 44% with sphincter dysfunction improved.
- Early diagnosis key “so large majority of patients able to walk and with good bladder function maintained these capacities”.
Radiation for Spinal Cord Compression

- Maranzano found neurologic recovery after “late” diagnosis was histology-dependent (myeloma, breast, prostate responded better than others). ([IJROBP] V32; 959-967, 1995).
- Maranzano also evaluated short-course RT in 53 patients with cord compression from “low radioresponsive” tumors (lung, H&N, GI, kidney, melanoma, sarcoma) or radioresponsive primaries (breast, prostate, myeloma, lymphoma) with paresis/plegia, poor Performance Status (ECOG ≥2)/short life expectancy.
- Patients received 8 Gy x 1; responders/stable disease got 8 Gy x 1 a week later (total 8 Gy x 2 over 1 week).
- Pain relief in 67%; “motor function response” 63%; 91% preserved ambulation; 98% preserved bladder function.
- Still, only 38% nonambulatory, 44% with bladder retention improved. ([IJROBP] 1997 Jul 15;38(5):1037-44).
Radiation for Cord Compression from Myeloma: Short Course vs. Long Course

- Retrospective review of 172 myeloma patients
  - (Int J Radiat Oncol Biol Phys 2006 64: 1452-1457)
- Short course RT: 8 Gy x 1; 4 Gy x 5 (n=61)
- Long course RT: 3 Gy x 10; 2.5 Gy x 15; 2 Gy x 20 (n=111)
- **Functional outcome** was evaluated
Improvement in motor function occurred in 90 patients (52%); 47% of nonambulatory patients regained the ability to walk.

Improvement in functional outcome was more frequent after long course RT than after short course RT: 59% vs. 39% (p=0.10) at 1 month; 67% vs. 43% (p=0.043) at 6 months; 76% vs. 40% (p=0.003) at 12 months; 78% vs. 43% (p=0.07) at 18 months; and 83% vs. 54% (p=0.33) at 24 months.

Similar functional outcome was seen with 3 Gy x 10 as 2.5 Gy x 15 and 2 Gy x 20

“Treatment with 10 x 3 Gy can be considered appropriate”.
Re-Irradiation for Spinal Cord Compression

- Recurrent spinal cord compression can occur after RT.
- Mayo reviewed their experience with re-irradiation on 54 pts. (*Ann Neuro* 1995 V 37, p. 583-589)
- Median first dose: 3000 cGy; median second dose: 2200 cGy; median combined dose: 5425 cGy
- All ambulatory after first RT; 74% ambulatory at time of 2nd RT; 78% ambulatory after reRT.
- 69% remained ambulatory at last FUP (88% preservation rate).
- Median survival only 4.2 months.
- 12% had neurologic deterioration; none “clearly” due to RT
Re-Irradiation for Spinal Cord Compression

Maximum stereotactic dose (to 95% isodose)
(BED = biologically equivalent dose; includes first RT + retreatment RT)

<table>
<thead>
<tr>
<th>Previous RT dose (BED in Gy(<em>2</em>))</th>
<th>6-9 months since last RT</th>
<th>&gt;9 months, &lt; 2 years since last RT</th>
<th>&gt;2 years since last RT</th>
</tr>
</thead>
<tbody>
<tr>
<td>30/10 (BED = 75)</td>
<td>25/10 (BED = 131)</td>
<td>27.5/10 (BED = 140)</td>
<td>30/10 (BED = 150)</td>
</tr>
<tr>
<td>37.5/15 (BED = 83)</td>
<td>22.5/10 (BED = 131)</td>
<td>25/10 (BED = 139)</td>
<td>27.5/10 (BED = 148)</td>
</tr>
<tr>
<td>40/20 (BED = 80)</td>
<td>22.5/10 (BED = 128)</td>
<td>25/10 (BED = 136)</td>
<td>27.5/10 (BED = 145)</td>
</tr>
<tr>
<td>45/25 (BED = 85.5)</td>
<td>22.5/10 (BED = 133)</td>
<td>25/10 (BED = 142)</td>
<td>27.5/10 (BED = 151)</td>
</tr>
</tbody>
</table>

Surgery for Cord Compression

- Surgery can often provide **quickest palliation.**
- Surgery can also obtain **tissue** if **diagnosis** unclear.
- Surgery necessary if **neurologic deterioration** despite RT or if compression is due to **bone fragments on cord.**
- Standard surgery has been **laminectomy.**
- **Vertebrectomy** may be appropriate for patients with solitary lesions and “significant” life-expectancy.
- **Post-operative radiotherapy** is usually delivered to treat residual/microscopic disease.
Surgery for Cord Compression: Patchell Study

- Patchell led a randomized trial comparing surgery followed by RT vs. RT alone for patients presenting with cord compression.
- Surgical intent was “to remove as much tumor as possible, provide immediate decompression, and stabilize the spine”.
- Same steroids, both groups got 30 Gy.
- Study stopped at interim analysis.
- **101 patients**: 50 surgery + RT; 51 RT only
Surgery for Cord Compression: Patchell Study

- More surgery patients were able to walk after therapy than RT patients: **84% vs. 57%** (p=0.001)
- Surgery patients **retained ability to walk longer**: 122 days vs. 13 days (p=0.003)
- Surgery patients **maintained continence** longer.
- Survival **NOT different**: 129 days surgery vs. 100 days RT
- 16 patients in each group entered study unable to walk – surgery patients had greater chance of **regaining walking ability**: 62% vs. 19% (p=.01)
- Less need for steroids and opioid analgesics in surgical group.
- Hospitalization length was 10 days for both groups.
Radiation for Nerve Root/Cauda Equina Compression

- Patients can have weakness due to spine tumors pressing on nerve roots or the *cauda equina*.
- **Cauda Equina Syndrome** consists of low back pain, unilateral/bilateral sciatica, saddle sensory dysfunction, bladder/bowel dysfunction (retention/constipation usually), and variable lower extremity weakness.
- **Lumbar spine tumors** can cause this (remember spinal cord ends around L1 in adults).
- Although not cord compression *per se*, we usually treat these emergently – earlier treatment = better chance for recovery.
Cauda Equina Compression from Lymphoma
Spinal Cord Compression: Topographic Anatomy Figure
Radiation for Palliation: The Quiz !!

John M. Holland, MD
OHSU Radiation Oncology
September 1, 2010
Don’t Sweat It!!
Here’s the Quiz!!!
Radiation for Palliation: The Quiz !!

1) What is the most common primary cancer to cause brain metastases?

- A) breast
- B) lung
- C) colorectal
- D) melanoma
Radiation for Palliation: The Quiz !!

1) What is the most common primary cancer to cause brain metastases?

Answer: B) lung
2) Which of the following primary tumors is MOST likely to present with HEMORRHAGIC brain metastases?

- A) renal
- B) lung
- C) breast
- D) colorectal
2) Which of the following primary tumors is MOST likely to present with HEMORRHAGIC brain metastases?

Answer: A) renal
Radiation for Palliation: The Quiz !!

3) According to Patchell’s Data, what is the median survival after resection of solitary brain metastasis followed by whole brain RT?

- A) 15 wks
- B) 25 wks
- C) 40 wks
- D) 75 wks
3) According to Patchell’s Data, what is the median survival after resection of solitary brain metastasis followed by whole brain RT?

Answer: C) 40 wks
Radiation for Palliation: The Quiz !!

4) According to Patchell’s second brain metastasis study, what was the benefit of adding whole brain RT after resection of a solitary metastasis?

A) improved survival  
B) increased “functional independence”  
C) decreased intracranial failure  
D) Please stop Dr. Holland, my brain pan is plum full with this here knowledge
Radiation for Palliation: The Quiz !!

4) According to Patchell’s second brain metastasis study, what was the benefit of adding whole brain RT after resection of a solitary metastasis?

Answer: c) decreased intracranial failure
Radiation for Palliation: The Quiz !!

5) In treating patients with multiple brain metastases with whole brain irradiation, which of the following is NOT true?

- A) Median survival is increased from 3 to 6 months
- B) Overall symptom response rate is 64-85%
- C) Cranial nerve dysfunction improves more readily than headache
- D) Many patients die from extracranial disease progression
Radiation for Palliation: The Quiz !!

5) In treating patients with multiple brain metastases with whole brain irradiation, which of the following is NOT true?

- Answer: c) cranial nerve dysfunction improves in about 40% but headaches improve in about 70%
6) Regarding radiation fractionation regimens for patients with multiple brain metastases, which of the following is NOT true?

A) Short schedules with large fractions result in quickest but least durable palliation.
B) RTOG “standard treatment” is 30 Gy/10 fxs
C) No schedule has proven superior in increasing overall survival
D) Death from brain metastases remains the overwhelming cause of death after cranial RT
Radiation for Palliation: The Quiz !!

6) Regarding radiation fractionation regimens for patients with multiple brain metastases, which of the following is NOT true?

Answer: d) Only about 40% of deaths are due to progressive CNS mets
7) Which of the following is NOT prognostically favorable in patients with brain metastases?

- A) KPS ≥ 70
- B) controlled primary
- C) age < 60 years
- D) lung primary
7) Which of the following is NOT prognostically favorable in patients with brain metastases?

- Answer: D) patients with lung cancer live a median of 13 wks. Breast cancer brain met patients live a median of 24 wks.
8) Regarding the addition of stereotactic radiosurgery to whole brain radiation for patients with 1-3 brain metastases, which of the following is NOT true?

- A) Patients with solitary mets had improved survival
- B) Younger patients (<50) had improved survival
- C) Adenocarcinoma histology was associated with improved outcome
- D) Radiosurgery patients were more likely to have stable/improved KPS at 3 months
Radiation for Palliation: The Quiz !!

8) Regarding the addition of stereotactic radiosurgery to whole brain radiation for patients with 1-3 brain metastases, which of the following is NOT true?

Answer: c) Squamous cell histology was associated with improved outcome
9) Which of the following cancers causes Superior Vena Cava Syndrome most frequently?

- A) Lymphoma
- B) Breast cancer
- C) Lung cancer
- D) Germ cell tumors
Radiation for Palliation: The Quiz !!

9) Which of the following cancers causes Superior Vena Cava Syndrome most frequently?

- Answer: c) 75% of SVC Syndrome is the result of lung cancer
Radiation for Palliation: The Quiz !!

10) Approximately what percentage of NSCLC patients with SVC Syndrome will respond favorably to palliative RT?

- A) 15%
- B) 25%
- C) 50%
- D) 80%
Radiation for Palliation: The Quiz !!

10) Approximately what percentage of NSCLC patients with SVC Syndrome will respond favorably to palliative RT?

Answer: c) Only 46% of NSCLC SVC Syndrome patients “achieve palliation” (compared with 62-80% response in small cell)
Radiation for Palliation: The Quiz !!

11) Approximately what percentage of patients with hemoptysis from lung cancer will respond to palliative radiation?

- A) 20%
- B) 40%
- C) 60%
- D) 80%
Radiation for Palliation: The Quiz !!

11) Approximately what percentage of patients with hemoptysis from lung cancer will respond to palliative radiation?

Answer: d) hemoptysis has 83% response rate to palliative RT
12) Regarding the use of radiation to relieve airway obstruction, which of the following is NOT true?

A) Only 23% overall achieve relief of atelectasis after RT

B) Atelectasis relief is more likely for small cell histology than NSCLC

C) Better outcome is associated with earlier radiation after lung collapse

D) Lung re-expansion will not occur after 2 weeks of collapse
12) Regarding the use of radiation to relieve airway obstruction, which of the following is NOT true?

- Answer: d) Re-expansion occurs in 23% after 2 wks compared with 71% if collapse within 2 weeks
Radiation for Palliation: The Quiz !!

13) Which of the following is the most significant side effect risk after endobronchial brachytherapy?

- A) hemoptysis
- B) esophagitis
- C) pneumonitis
- D) nausea
13) Which of the following is the most significant side effect risk after endobronchial brachytherapy?

- Answer: a) hemoptysis. Fistulae also occur.
14) Which is the MOST likely to be palliated with radiation?

A) pain from carcinomatous brachial plexopathy
B) hoarseness from recurrent laryngeal nerve impingement due to NSCLC
C) Dr. Holland, you lazy S.O.B., are there only two choices for this question?
Radiation for Palliation: The Quiz !!

14) Which is the MOST likely to be palliated with radiation?

Answer: a) pain from carcinomatous brachial plexopathy (77% according to Ampil)
Radiation for Palliation: The Quiz !!

15) Approximately, what percentage of patients with dysphagia from esophagus cancer will be palliated with RT?

- A) 10%
- B) 30%
- C) 50%
- D) 80%
Radiation for Palliation: The Quiz !!

15) Approximately, what percentage of patients with dysphagia from esophagus cancer will be palliated with RT?

- Answer: d) 80-89% palliation rates are reported (often this palliation is short-lived)
Radiation for Palliation: The Quiz !!

16) Which is the least likely complication of endoluminal HDR brachytherapy when treating esophageal cancer?

A) stricture
B) ulcer
C) fistula
D) hematemesis
Radiation for Palliation: The Quiz !!

16) Which is the least likely complication of endoluminal HDR brachytherapy when treating esophageal cancer?

Answer: d) hematemesis
Radiation for Palliation: The Quiz !!

17) Approximately what percentage of patients with cervix cancer will have successful palliation of bleeding with RT?

- A) 20%
- B) 30%
- C) 50%
- D) 90%
17) Approximately what percentage of patients with cervix cancer will have successful palliation of bleeding with RT?

Answer: d) 90%
Radiation for Palliation: The Quiz !!

18) What dose of radiation did Lingareddy use to treat symptomatic rectal cancer progressing after previous RT?

A) 15 Gy
B) 20 Gy
C) 30 Gy
D) 50 Gy
Radiation for Palliation: The Quiz !!

18) What dose of radiation did Lingareddy use to treat symptomatic rectal cancer progressing after previous RT?

Answer: c) 30.6 Gy
Radiation for Palliation: The Quiz !!

19) When using radiation for palliation in recurrent rectal cancer, which of the following is LEAST likely to be successfully palliated?

- A) rectal bleeding
- B) pain
- C) mass effect
Radiation for Palliation: The Quiz !!

19) When using radiation for palliation in recurrent rectal cancer, which of the following is LEAST likely to be successfully palliated?

Answer: c) mass effect

“bleeding 100%, pain 65%, mass effect 24%”
Radiation for Palliation: The Quiz !!

20) According to RTOG study, when using radiation for palliation of liver metastases, which of the following is NOT true?

• A) Whole liver RT was 21 Gy/ 3 Gy fxs
• B) 80% achieved symptomatic improvement
• C) Complete pain relief occurred in 54%
• D) Liver mets from lung primaries are best palliated
Radiation for Palliation: The Quiz !!

20) According to RTOG study, when using radiation for palliation of liver metastases, which of the following is NOT true?

Answer: d) colon cancer mets to liver had best palliation
Radiation for Palliation: The Quiz !!

- 21) TRUE or FALSE: Metastatic disease in weight bearing areas associated with greater than 50% cortical bone destruction should undergo orthopedic evaluation for surgical stabilization.
21) TRUE or FALSE: Metastatic disease in weight bearing areas associated with greater than 50% cortical bone destruction should undergo orthopedic evaluation for surgical stabilization.

Answer: True
Radiation for Palliation: The Quiz !!

22) What is the usual first sign of cancer causing spinal cord compression?

A) pain
B) paralysis
C) a lumpy in the PJs
D) telephone call Friday @ 4 PM
Radiation for Palliation: The Quiz !!

- 22) What is the usual first sign of cancer causing spinal cord compression?

- Answer: a) pain  Patients with cancer and back pain need spine imaging (MRI is best)
Radiation for Palliation: The Quiz!!

23) Where in the spinal column is spinal cord compression from cancer most likely to occur?

- A) cervical
- B) thoracic
- C) lumbar
- D) sacral
23) Where in the spinal column is spinal cord compression from cancer most likely to occur?

Answer: b) thoracic spine
24) Approximately how many patients with spinal cord compression from cancer will have neurologic progression during the course of palliative RT?

- A) 5%
- B) 10%
- C) 25%
- D) 50%
24) Approximately how many patients with spinal cord compression from cancer will have neurologic progression during the course of palliative RT?

Answer: 25% “Of 100 patients with cord compression, radiation will be completed on 60; 20 patients will progress (neurologic deterioration) during RT; 20 will not be referred due to total paralysis or imminent death.”
25) TRUE or FALSE: Most non-ambulatory patients with spinal cord compression regain the ability to walk after RT.
25) TRUE or FALSE: Most non-ambulatory patients with spinal cord compression regain the ability to walk after RT.

Answer: False. While most walking patients maintain function, in Maranzano’s series, only 38% non-ambulatory patients improved after RT.
Radiation for Palliation: The Quiz !!

26) After successfully treating malignant spinal cord compression with RT, what is the approximate risk of RECURRENT spinal cord compression?

- A) 5%
- B) 10%
- C) 20%
- D) 40%
26) After successfully treating malignant spinal cord compression with RT, what is the approximate risk of RECURRENT spinal cord compression?

Answer: B) Loeffler reports 11.3% risk of recurrent compression after RT
Radiation for Palliation: The Quiz !!

27) Which of the following is the most reasonable alpha/beta for spinal cord?

- A) 2
- B) 5
- C) 7
- D) 10
Radiation for Palliation: The Quiz !!

27) Which of the following is the most reasonable alpha/beta for spinal cord?

Answer: a) 2 (sometimes radiobiologists will use alpha/beta of 3 for CNS)
Radiation for Palliation: The Quiz !!

28) According to Patchell’s spinal cord compression study, patients receiving surgery followed by RT have all of the following improvements over RT alone EXCEPT:

- A) retained ability to walk longer
- B) maintained continence longer
- C) improved survival
- D) more likely to regain ability to walk
28) According to Patchell’s spinal cord compression study, patients receiving surgery followed by RT have all of the following improvements over RT alone EXCEPT:

- Answer: c) survival was no different in patients treated with surgery + RT vs. RT alone: surgery 128 days vs. RT 100 days
29) Which of the following is not typically seen in cauda equina syndrome?

A) low back pain 
B) saddle sensory loss 
C) bladder/bowel dysfunction 
D) arm weakness
29) Which of the following is not typically seen in cauda equina syndrome?

- Answer: d) arm weakness is not typically seen in cauda equina syndrome. (Not all of ‘em have to be hard!)
Radiation for Palliation: The Quiz !!

30) The angle of Louis (approximately) corresponds to what vertebral level?

A) Top of T2
B) Top of T4
C) Top of T6
D) Top of T8
Radiation for Palliation: The Quiz !!

30) The angle of Louis (approximately) corresponds to what vertebral level?

Answer: c) Top of T6

The suprasternal notch is at the top of T4; the xiphoid tip is at the top of L1.
Radiation for Palliation: The Quiz !!

31) Which of the following is NOT true regarding RTOG 9714, a phase III trial comparing 8 Gy x 1 vs. 30 Gy in 10 fractions in the treatment of bone metastases?

- A) Eligible patients had breast or prostate cancer
- B) Acute toxicity was greater after 8 Gy x 1
- C) Overall response rate was 66%: 17% CR, 49% PR
- D) At 3 months, there was no difference in pain and narcotic use relief between the two study arms
31) Which of the following is NOT true regarding RTOG 9714, a phase III trial comparing 8 Gy x 1 vs. 30 Gy in 10 fractions in the treatment of bone metastases?

- Answer: B. **Acute grade 2-4 toxicity** was significantly **higher** in the **30 Gy in 10 fraction** arm: 17% vs 10% (p<0.0001).