Metastatic Spine Disease Management Options: An Integrated Approach

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The Problem

- 60 - 84% of pts with solid tumors develop bone metastases
- Lung > Liver > Skeleton
- Spine > 50%
- Survival and disease control rate steadily improving with ~60% of patients surviving 5+ years
- Tx of both symptomatic and asymptomatic spinal metastases is of increasing clinical importance

Prognosis

- Median survival for patients with metastatic disease is 10 months
- Death typically results from systemic malignancy
- Spinal vertebral metastases commonly signals disseminated disease
- In the past, ? role for treatment

Prognosis Cont’d

- BUT treatment is warranted especially for Quality of Life (rather than cure)

GOALS

- Preservation or restoration of ambulation
- Bladder control
- Pain Relief

Effective Treatment

- Often requires
  - Multidisciplinary therapies (medically challenging, individually tailored)
  - Understanding of the clinical condition (bony stability, compression of neural structures, tumor radiosensitivity)
  - Life Expectancy assessment
  - Specific attention to QOL of the patient

The 2 Game Changers

- Decompressive Surgery
- Spine Radiosurgery
Surgery

- Surgical treatment for spine metastases widely abandoned when conventional radiation was compared to laminectomy
- Beginning in 1980's, new surgical approaches and improved instrumentation for stabilization and fusion changed the trend towards surgery

Treatment Strategies

- Surgical Techniques predominantly have a role in decompression of the spinal cord and mechanical management/spine stabilization
- What about the Oncological Aspects of Spine metastases?
  - Durable Local Tumor Control

Local Control

Surgery

- improves the chance of neurological recovery in patients with high grade cord compression
- restores spine stability

BUT

Stereotactic Radiosurgery

Dual Requirement of Effective Spine Metastatic Tumor Treatment

1) **Pain** Palliation (or **Pain** Prevention)

2) **Tumor control** and prevention of neurological compromise

Achieved either through monotherapy or as part of combination/multimodality treatment
Stereotactic Radiosurgery

- Delivery of an accurate and conformal high radiation dose to the tumor
- Delivered in 1-5 sessions
- Steep fall-off dose gradients associated with the treatment protects the adjacent normal structures

Essential Improvements

- Modulated Radiation delivery (Intensity Modulated Radiation Therapy – IMRT or Volumetric Modulated Arc Therapy - VMAT)
- High Resolution Imaging
- Adequate and appropriate spine immobilization
- Target localization (imaging for position verification and if necessary adjustment before or during treatment)

Spine Radiosurgery Process

- Immobilization & CT simulation
- High Definition MRI scan
- Target Identification
- Treatment Planning
- Physics plan verification (Phantom Run)
- Patient Localization
- Radiation delivery

2 hours
2-3 days
1-2 hours

Neurosurgeon (Radiation Oncologist, Physicist, Therapist (Nurse))

Candidates for Spinal Radiosurgery

- Patients with pain or tumor progression
- Minimal to moderate spinal cord compromise
- May be previously irradiated lesions
- Residual or recurrent after surgical therapy
- Difficult surgical approaches
- Relative short life-expectancy for metastases
- Significant medical co-morbidities

Case Example: Melanoma

- 33 y.o male
- Metastatic Melanoma C3
- Surgical instumentation with minimal tumor debulking
- Persistent pain 7/10 (narcotics)
- Single fraction 14 Gy
- 5.5 years no pain, disease site remains controlled

64 y.o. M with L2/3 RCC metastasis Tx with 14 Gy

Baseline pain score: 4.3 (Roxanol 10 mg 5x/Day)
1 month pain score: 3.1 (Advil 200 mg daily)
9 months pain score: 0 (no meds)* (47%)

*[score of 0 (no meds) from 3 months]
Case Example: Renal Cell Carcinoma

- 60 y.o male presenting a renal mass and L3 pathological fracture
- Pain 6/10 (on Morphine)
- SRS single fraction (14 Gy)
- Week 1: BPI (pain scores) decreased by 33%

Case Example: Renal Cell Carcinoma

- Pain recurred
- Imaging studies at 3 months post SRS:
  - Decrease in size and signal abnormality of metastatic involvement of L3
  - Worsening compression fracture
- Underwent vertebral augmentation
- Biopsy showed only very few atypical carcinoma cells

Case Example: Small Cell Lung Ca

- 53 y.o male presenting small cell lung cancer
- Prior irradiation to met in retromolar area and also WBXRT with post fossa boost
- Pain 7/10 (on Oxycontin)
- SRS single fraction (10 Gy)
- Week 1: BPI (pain scores) decreased by 67% with narcotic dose also decreased by 63%

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Review of Literature for SRS Outcomes

- Local tumor control
  - MSKCC 90%
  - MD Anderson 84%
  - Pittsburgh (500 cases) was 88.95

- Pain relief
  - 84 - 100% pain
**Pain Medication Use Over Time**

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**EORTC QLQ-C30 Symptom Scales**

### QOL Over Time (mean ± s.d)

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<td>Insomnia p &lt; 0.006</td>
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<td>Pain p 0.02</td>
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<td>Constipation p &lt; 0.004</td>
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**Major potential benefits of SRS**

- Short treatment time in an outpatient setting
- No recovery time
- Good symptomatic response
- Successful tumor control
- Low morbidity

**Contraindications for SRS**

- **Rapidly** progressive neurological deficit
- Cord compression by bone or disk fragments
- No known cancer tissue diagnosis
- * Overt spine instability

**How Good Are We in Terms of Clinical Safety?**

- Series of 500 patients with no evidence of radiation-related myelopathy (Gerszten et al. Spine, 2007)
- Series of 230 procedures in 177 patients and reported only one case of radiation-related myelopathy improved on dexamethasone (Ryu et al. Cancer, 2007)
- Delayed radiation-induced myelopathy after SRS 6 cases in 1075 pt, 3 patient who had prior radiation (Gibbs et al NSx, 2009)
**Key to Treatment Safety**

- Careful dose constraint to the adjacent spinal cord
- Radiation Myelopathy as a late toxicity with overdosing spinal cord with modern era conventional fractionated XRT is very uncommon
- We must monitor that this does not re-emerge with SBRT

**Keys to Treatment Safety**

- “Separation” surgery (SS)
  - Surgery as an adjunct to the definitive procedure of radiosurgery

**Impact of SS surgery on spinal cord dosing with SRS**

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<th>Post SS (actual tx at 16 Gy)</th>
<th>No SS (mock tx at 16 Gy)</th>
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**The Next Step**

**WHAT ABOUT Combination Therapy?**

**Reasons of Combination**

- Appropriate Pain control
- Local control
- Separation
- Fusion rate
- Wound integrity
Pain Characterization

• Biological Pain
  – Nocturnal
  – Resolves with Steroids

• Mechanical Pain
  – Instability related
  – Movement related pain
  – Surgery should be considered

Mechanical Instability

• AA: Rotational pain
• Cervical: Flexion/Extension pain
• Thoracic: Extension (pt sleep upright in chair)
• Lumbar: Mechanical Radiculopathy with axial loading (Searing leg pain on sitting or standing)

Spinal Oncology has addressed Mechanical Instability with …

• New instrumentation in spinal reconstruction
• New surgical approaches to the spine (combined anterior/posterior resections)
• Complication avoidance
• Trend towards “minimally invasive” techniques (vertebral augmentation)

Surgery and SRS combinations have provided effective synergistic efficacy

• Open surgery & instrumented fusion
• Separation surgery (SS)
• Vertebral augmentation and SRS

Surgery and SRS

• Moulding et al (2010): 21 patients operated and received adjuvant SRS
• Single-fraction high-dose spinal radiosurgery (dose range 18–24 Gy, median 24 Gy)
• actuarial rates with a 1-year probability of local control of 90.5%.
• Spine radiosurgery after surgical decompression and instrumentation for tumor is a safe and effective technique that can achieve local tumor control until death in the vast majority of patients

Surgery and SRS

• Rock et al (2006): 18 patients operated and received adjuvant SRS
• Various open surgical procedures (corpectomy, laminectomy)
• Local control appears to be excellent
• 92% of patients with initial neurologic deficit, improved or remained stable (median fu 7 months); Reminder: 57.9% recurrence at 6 months Sx and EBRT

Surgery and SRS
Surgery and SRS

CCF experience

• 17 patients were operated with or without instrumentation/fusion
• All were treated with adjuvant SRS
• All were followed with a MRI allowing for local control assessment
• Mean f/u 17 months
• 1 patient had radiologic recurrence, 2 had clinical recurrence (pain) [95% radiographic control; 90 pain control]
• Mean volumetric tumor size decrease was 17%

Surgery and SRS

• Laufer et al. evaluated local disease control for spinal metastases following “separation surgery” and adjuvant hypofractionated or high-dose single-fraction SRS in 186 patients
• The overall local progression rate after radiosurgery was 16% at 1 year.
• Only factor significantly associated with 1-yr local tumor progression was the postoperative radiosurgical radiation (HD-hypoF 4%, LD-hypoF 22% single-F 9%)

Decompression/Instrumented Fusion and SRS

• Evaluate the effect of the type of radiation delivered on fusion rates and instrument failure post open surgical decompression

Reminder: Patients are surviving longer…..

We should consider the Intermediate
Consequences and Outcomes of our
Interventions

Decompression/Instrumented Fusion and SRS

• Surgical decompression and stabilization, combined with radiation or radiosurgery, is an effective management option for patients with metastatic spine disease
• Well known that radiation can weaken bones and impair normal healing
• Spinal radiosurgery (SRS) delivers high dose focal radiation to the tumor region
• As a consequence of this focal delivery, there is a partial sparing of the juxtaposed tissues, such as the instrumented construct and bone graft

Decompression/Instrumented Fusion and SRS

• The Cleveland Clinic Spine Tumor board (2006-2009) prospectively collected patient information (925 spine patient database)
• Patients who underwent spine surgery with instrumentation (with or without bone graft) followed by radiation or radiosurgery within 2 months
• Further, each patient then required a minimum follow-up of 6 months post surgery to be included in the series
  — to appropriately assess the primary outcome of instrumentation failure or proof of fusion.

1) WORLD NEUROSURGERY 74 (4): 517-532, OCTOBER/NOVEMBER 2010
g5 insert ref
generic, 3/19/2010
Decompression/Instrumented Fusion and SRS

- 15 instrumented patients received post-operative irradiation
- 8 radiosurgery; 7 conventional radiation
- Conventional radiation group, 43% of patients had instrumentation failure,
- SRS group no instrumentation failure (p=0.08)
- Excluding the instrumentation only patients, fusion rate was 50% in the radiosurgery group compared with 17% in the conventional group (NS)

Conventional Radiation and Instrumented Fusion Failure

- 38 y.o. M.
- C3 malignant nerve sheath tumor
- Resection and instrumented fusion (combined ventral and dorsal approach)
- Post-operatively treated with conventional radiation (56Gy in 2Gy fractions)
- 20 months after surgery returned with neck pain

Conventional Radiation and Instrumented Fusion Failure

- left C1 screw breakage
- lucency around the right screw and left screw

Surgery Followed by SRS

- 58 y.o. M with C3 chordoma
- Resection and instrumented fusion with a combined ventral and dorsal approach
- SRS 16 Gy in a single fraction
- Blue is the 16 Gy prescription isodose line, Green is the 12 Gy dose fall off region
- There is relative sparing of the dorsal fusion surface from radiation as the 12Gy isodose line is ventral to the fusions laterally
- As early as 5 months post-operatively, fusion was evident on imaging in this patient

Decompression/Instrumented Fusion and SRS

- Precisely delivering ionizing radiation to tumors while sparing the surrounding organs or vital structures
- Well documented effects of conventional radiation therapy on bone healing
- Should a fusion site should also be considered an organ at risk (OAR)?
- This preliminary data clearly shows a trend towards higher fusion rates and a lower incidence of instrumentation failure with SRS vs. conventional radiation therapy
- Larger prospective studies needed

Spine Radiosurgery Options

1) Stand alone procedure
2) Component of combination therapy
   - Open surgery and instrumented fusion
   - Separation surgery (SS)
   - Vertebral augmentation and SRS
Vertebral Augmentation
PETER C. GERSZTEN et al
J Neurosurg Spine 3:296–301, 2005

- 26 patients (mean age 72), mixed histologies with 11 lung
- Pathological compression fractures (16 thoracic and 10 lumbar) were prospectively evaluated
- Underwent kyphoplasty that involved the percutaneous transpedicular technique followed by SRS (mean 12 days after kypho)
- Axial pain improved in 24 (92%) of 26 patients.
- New treatment paradigm combining kyphoplasty and spinal radiosurgery was found to be clinically effective
- Now 2 minimally invasive surgical procedures are combined to avoid the morbidity associated with open surgery
- Combination therapy resulted in immediate fracture fixation oncological control
- NO radiation toxicity and new neurological deficit from combination

Rose et al JCO 27(30) 5075-5079, 2009

Fracture Risk after single session SRS
- 62 consecutive patients, 71 levels
- Fracture progression was noted in 27 vertebrae (39%)
- Lytic lesions involving >40% of VB were 6.8 X more likely to fracture than were sclerotic and mixed lesions (95% CI, 1.4 to 33.3)
- Lesions located between T10 and the sacrum were 4.6 X more likely to fracture than were lesions above T10 (95% CI, 1.1 to 19.7)
- ??? Role of prophylactic stabilization

Boehling et al

- Evaluated patient post SRS for compression fractures
- 93 patients, 123 levels.
- SRS 1, 3, or 5 fractions for overall median doses of 18, 27, and 30 Gy, respectively
- The median imaging follow-up was 14.9 months (range 1–71 months)
- 25 new or progressing fractures (20%) were identified, and the median time to progression was 3 months after SBRT
- Multivariate analysis:
  - Age > 55 years (HR 10.66, 95% CI 2.81–40.36)
  - Preexisting fracture (HR 0.17, 95% CI 2.31–36.43)
  - Baseline pain (HR 1.41, 95% CI 1.05–1.9)
- Obesity (HR 0.02, 95% CI 0–0.2) was protective (?) Increased bone density
- ? Prophylactic vertebral augmentation

Cunha et al
IJROBP 2012.04.034

- Evaluated patient post SRS for compression fractures
- 90 patients, 167 levels
- Median follow-up was 7.4 months
- 11% 12 de novo fractures (63%) and 7 cases of fracture progression (37%) The mean time to fracture after SBRT was 3.3 months (range, 0.5-21.6 months)
- The 1-year fracture-free probability was 87.3%
- Multivariate analysis confirmed:
  - alignment P=.0003 presence of kyphotic/scoliotic
  - lytic lesions (P=.007), lung (P=.03) and hepatocellular (P=.0001) primary histologies (P<.004)
  - Dose per fraction of 20 Gy or greater (P<.004)
- ? prophylactic treatment versus dose modification

Vertebral Compression Fracture After Spine Stereotactic Body Radiotherapy: A Multi-institutional Analysis With a Focus on Radiation Dose and the Spinal Instability Neoplastic Score

- Multi-institution study of VCF after SBS (UofT, CCF, MDA)
- 252 pts; 410 spinal segments
- Assessed development of new VCF or progression of baseline VCF
- Median flu: 11.5 months (range, 0.03 to 113 months)
- S7410; Rate 14% (47% new, 53% progression)
- median time to VCF was 2.46 months (range, 0.03 to 43.01 months); 63 % in 1st 4 months
- dose per fraction (greatest risk for ≥ 24 Gy or 20 to 23 Gy ≤ 19 Gy) by MRA
- three of the six original SINS criteria: i) baseline VCF, ii)lytic tumor, and iii)spinal deformity, significant predictors of VCF.

Role of **Prophylactic** Augmentation in Spine Mets

- No prospective trials
- No retrospective studies
- Premature to consider
- Radiographic VCF ≠ Symptomatic VCF

VA Future Options ???

- Radioisotopes + VA (¹⁰⁹Y, ³²P,¹⁵³Sm-EDTMP mixed with PMMA)
- RFA + VA
- Chemotherapy + VA

Summary

- SRS results in rapid and durable control in terms of
  - Pain Control
  - Radiographic Control
- Effective stand-alone treatment modality
- Role in multimodality treatment of spine tumors

How best to treat spine metastases?

Treatments for Spinal Metastases

- Analgesics, Bracing & Bedrest (?role)
- Radiation/Radiosurgery
- Chemotherapy
- Surgery
  - Curative
  - Palliative
  - Prophylactic
  - Reconstructive
Summary

• With improvements in systemic as well as supportive therapies for cancer, patients who have bony metastases are surviving substantially longer.

• The care of these patients is complex!

• A few treatment algorithms have been proposed for patients with spine metastases but no formal treatment guidelines are available.

• A multidisciplinary team approach is needed for optimal assessment and treatment recommendations.

• As well, timely and often multimodality interventions are essential to decreasing morbidity in these patients and to maintain QOL.

QOL with SRS

• 52 y.o M
• Papillary carcinoma of the thyroid
• T9 hemi-corpectomy 1/05
• 2/06 recurrence on PET (SUV 7.1)
• SRS 14 Gy single fraction in February 2006

QOL Achieved!

• 5 years f/u
• Disease stable on serial MRI imaging
• SUV 3.9 (initial 7.1)
• Fully active

TEAMWORK