Charged Particle Radiation Therapy in the Treatment of Bone and Soft Tissue Sarcoma

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Management of Sarcomas

• Multidisciplinary approach
  – Contemporary management of sarcomas requires a multidisciplinary approach, often using a combination of surgery, radiation, and chemotherapy specific for tumor type, histologic grade, and stage of disease.
Management of Sarcomas

• Specialized expertise
  – These tumors are relatively uncommon and present in a variety of anatomic sites
    • Hence, most clinicians see them infrequently
  – Because successful treatment with good functional outcome often requires appropriate multidisciplinary expertise, referral to centers with experienced sarcoma teams is the most appropriate management strategy
Local Recurrence of Soft Tissue Sarcomas after Surgery

- Related to infiltration of tumor cells into peri-tumoral tissue beyond the gross tumor
  - Invade locally along anatomic planes (muscle fibers, neurovascular bundles, fascial planes)
  - LN involvement uncommon (5% overall)
- Exceptions: Synovial, Clear cell, Angiosarcoma, Rhabdoyosarcoma, Epithelioid
Wide Surgery Alone for Extremity and Truncal Sarcoma

- Appropriate for
  - Superficial low grade lesions ≤ 5 cm that can be widely excised
  - Selected larger low grade lesions
  - Selected superficial intermediate and high grade lesions ≤ 5 cm

- Most intermediate and high grade lesions > 5 cm will be considered for adjuvant radiotherapy
MRI Assessment of Extent of Tumor

• White et al (Princess Margaret)
  – Assessed MRI and pathology in 15 STS patients undergoing surgery
  – Tumor cells beyond main mass in 10/15
    • 6 pts < 1cm
    • 4 pts 1-4 cm
    • In 9/10, in area of T2 edema, which was usually proximal/distal to tumor
      – IJROBP 61:1439, 2005

• A: T1
• B: T2
  ← = edema
• C: T1 + g
Fig 5. Local recurrence-free survival of patients with low-grade extremity tumors treated with surgery alone, or surgery and postoperative adjuvant XRT.
Fig 2. Local recurrence-free survival in patients with high-grade, locally resectable extremity soft tissue sarcomas randomized to treatment with surgery and adjuvant chemotherapy versus surgery, adjuvant chemotherapy, and postoperative XRT. LR occurred only in the absence of XRT.
Impact of Local Recurrence

• Pisters et al (Memorial Sloan Kettering)
  – Analysis of prognostic factors showed that presentation with local recurrence was adverse factor for distant recurrence and disease-specific survival
    • J Clin Oncol 1996; 14:1679.

• Eilber et al (UCLA)
  – Patients with high grade STS who suffer a local recurrence are ~ 3 x higher risk of sarcoma death vs. patients with local control
Bone Sarcomas

• Surgery
  – Treatment of the primary lesion for most patients
    • Acceptable margins difficult to achieve in the axial skeleton including skull, spine, sacrum, and pelvis
    • These are sites where radiation can be important component of local control
Radiation Strategies

• Integration of Radiation Therapy
  – Radiotherapy can be employed as neoadjuvant (pre-operative), adjuvant (post-operative), or primary local therapy depending upon the site and type of tumor, the availability and acceptability of the surgical option, and the efficacy of the chemotherapy
Radiation Strategies

• Neoadjuvant (pre-op) Radiation Therapy
  – Frequently employed for large, deep soft tissue sarcomas
  – Can also be delivered prior to resection of spine or pelvic sarcomas.
  – Can be advantageous to facilitate resection, reduce risk of wound seeding, and minimize radiated volume
Radiation Strategies

• Adjuvant (post-op) Radiation Therapy
  – Following resection of soft-tissue sarcoma if tumor or surgically contaminated tissues in patients with incomplete excision, can not be excised with \( \geq 1 \) cm margin or an intact fascial plane.
  – Bone sarcomas with (+) or inadequate margins
    • Presentation with a pathologic fracture
    • Close margin and poor histologic response to chemoRx
    • Intralesional excision of or intramedullary rod placement through a radiographically or cytologically benign-appearing lesion later found to be sarcoma
Radiation Strategies

• Definitive (Primary) Radiation Therapy after Biopsy or Subtotal Resection
  – Medically inoperable patients
  – Axial or extremity Ewing sarcomas where surgery would compromise function
  – Primary bone tumors involving upper sacrum, portions of the pelvis, the base of skull, and ethmoid/sphenoid sinus.
Radiation Strategies

- External beam
  - 3D
  - IMRT
  - Charged particles
- Brachytherapy
- Intraoperative radiation therapy
  - Retroperitoneal
  - Extremity
Radiation Dose- Sarcomas

- Soft Tissue Sarcomas
  - The radiation sensitivity of soft tissue sarcomas similar to breast and other epithelial tissues.
  - Pre-operative adjuvant radiation doses of 50 Gy or post-operative radiation therapy doses of 60 Gy are associated with local tumor control rates > 90% in patients with extremity lesions resected with negative margins.
Radiation Dose- Sarcomas

• Soft Tissue Sarcomas
  – Radiation therapy provides local control of 
    ~75% of patients with soft tissue sarcomas 
    resected with positive margins
  – Doses of 66-68 Gy are recommended
  – Doses of ≥ 65 Gy are associated with 
    higher rates of local control and reported to 
    be as high as 85% in MGH data (DeLaney 
    et al, IJROBP 2007;67:1460)
### Unresected Soft Tissue Sarcomas

- **Massachusetts General Hospital**
  - 112 patients with unresected sarcomas 1971-2001

<table>
<thead>
<tr>
<th>Tumor Size</th>
<th>&lt; 63 Gy</th>
<th>&gt; 63 Gy</th>
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<tbody>
<tr>
<td>≤ 5 cm</td>
<td>22%</td>
<td>72%</td>
</tr>
<tr>
<td>&gt;5 cm ≤ 10 cm</td>
<td>49%</td>
<td>42%</td>
</tr>
<tr>
<td>&gt;10 cm</td>
<td>0%</td>
<td>25%</td>
</tr>
</tbody>
</table>

\[ p = 0.08 \quad p < 0.05 \]

Radiation Dose- Sarcomas

- **Ewing’s Sarcoma**
  - Surgery preferred for lesions that can be excised with acceptable morbidity
    - Microscopic residual disease is usually treated to 50.4 Gy.
  - Radiation sensitive
    - James Ewing: radiation sensitivity of this tumor was one of the features distinguishing it from other bone sarcomas
  - Gross disease
    - 55.8 Gy in association with chemotherapy
    - Consideration of higher doses for high risk bulky axial tumors i.e. pelvis is reasonable
    - Vertebral lesions traditionally treated to only 45 Gy
Radiation Dose- Sarcomas

- **Chondrosarcomas and Osteosarcomas**
  - Microscopic residual disease ~ 66 Gy
  - Gross residual disease ≥ 70 Gy

- **Chordomas**
  - Microscopic residual disease ~ 70 Gy
  - Gross residual disease > 75 Gy
Protons: Physical Dose Advantage

• Clinical advantage for protons over photons is a physical advantage based upon the superior dose distributions which can be achieved with protons

• Lower normal tissue doses for any tumor dose
  – Slightly higher skin surface dose compared to photon
Protons: Physical Dose Advantage

• Protons deliver more conformal doses than 2-D or 3-D radiation techniques
  – Allows higher doses to tumor target
    • Improved local control
    • Improved survival
  – Reduces dose to normal tissue
    • Reduction in acute morbidity
      – Fewer interruptions in radiation, chemotherapy
        • Improved local control, survival
    • Reduction in late morbidity
Protons: Physical Dose Advantage

- Intensity modulated radiotherapy (IMRT)
  - Target dose distributions similar to protons
    - Integral dose is ALWAYS higher than with protons
    - Although selected normal tissues can be spared with IMRT, this is at the cost of INCREASED DOSE TO OTHER NORMAL TISSUES
      - No advantage to the patient for irradiation of normal tissue
      - How high is the clinical toxicity of IMRT low-moderate dose bath

- Proton cost ~ 2.4 fold higher than IMRT photons
  - Future efficiency gains might decrease this to 1.7
  - Important to define appropriate indications

- INTENSITY MODULATION IS APPLICABLE TO PROTONS
Protons: Radiation Biology

• Low LET (linear energy transfer) radiation
  – Ionization with similar biologic effect to photons
  – Relative Biologic Effect (RBE) is ~1.1 vs. $^{60}\text{Co}$
  – Proton doses: cobalt gray equivalents (CGE)
    • CGE = physical dose in Gray x 1.1 (RBE correction)
  – Protons have been successfully combined with photons in reasonably straightforward manner
    • Many reported results are combined photon-proton results
Sarcomas of the Spine

- Rare: ~ 200 cases per year in the U.S.
  - Chordomas
  - Chondrosarcomas
  - Osteosarcomas
  - Ewing’s sarcoma
  - Giant cell tumor
Challenges in Managing Spine Sarcomas

• Surgical
  – Oncologic ideal of achieving a resection with negative margins through an approach that does not violate tumor or pseudocapsule rarely possible
    • Extraosseous extension frequent
    • Involvement of adjacent mediastinal/retroperitoneal structures, as well dura and spinal cord
    • Tumor cell often in direct contact with dura, thereby invading it on microscopic basis
    • Resection/disruption of dura can seed tumor into CSF
Sarcomas of the Spine

• Low rates of control with standard therapy
  – Osteosarcoma
    • 15/22 (68%) local failure (Ozaki, 2002)
    • Contrast with extremity where local control > 90%
  – Chondrosarcomas
    • 3/14 (21%) local failure after en bloc excision but 10/10
      (100%) local recurrence after piecemeal excision (Boriani et al, Bologna)
  – Chordoma
    • 75% Local failure (Mayo Clinic)
Challenges in Managing Spine Sarcomas

- Radiation therapy
  - Effective adjuvant therapy for sarcomas
  - Proximity of spinal cord make dose delivery difficult with conventional 3D radiation therapy
  - IMRT and imaged guided techniques have facilitated delivery of higher doses
Sarcomas of the Spine

- Hug et al. (Harvard Cyclotron Laboratory)
  - Photon/proton XRT +/- resection 1980-1992
    - 47 pts: osteogenic/chondrogenic axial skeletal tumors
    - XRT: Post-op (n=23), Pre + post-op (n=17), XRT only (7)
      - Group I: Chordoma/Chondrosarcoma n=20
        - Mean 73.9 CGE 5 Year LC 53%/100%
      - Group II: Osteosarcoma n=15
        - Mean 69.8 CGE 5 Year LC 59%
      - Group III: Giant cell tumor, osteo or chondroblastoma n=12
        - Mean 61.8 CGE 5 Year LC 83%
    - Trend to improved LC: primary, > 77 Gy, less residual
Sacral Chordoma

- Park L, DeLaney TF, Liebsch NL, et al (MGH)
  - 21 patients: Surgery + photon/proton XRT
    - Local control
      - 12/14 for primary lesions
      - 1/7 for recurrent lesions
  - 6 patients: Photon/Proton XRT
    - Local control
      - 3/6 all patients
      - 3/4 patients who received ≥ 73.6 Gy (35-91 months)
Phase II Study of Proton Radiation Therapy for Spine and Paraspinal Sarcomas

TF DeLaney, NJ Liebsch, IJ Spiro, PL McManus, JA Adams, S Dean, FJ Hornicek, FX Pedlow, AL Rosenberg, GP Nielsen, DC Harmon, SS Yoon, KA Raskin, HD Suit
Clinical Trial

• Phase II Clinical Trial for Spine/Paraspinal Sarcoma (PI T. DeLaney MD)
  – Surgery + IORT (Dura Plaque) + Photon/Proton
    • Surgery: Maximal debulking/spine stabilization
    • IORT: $^{90}$Y dural plaque: 10 Gy
    • Photon/Proton Radiotherapy
      – 70.2 GyE (Microscopic residual)
      – 77.4 GyE (Gross residual disease)*
      * Concurrent chemotherapy, diabetes: 70.2-72 GyE
      * Giant cell tumor, Ewing’s Sarcoma: 61.2 GyE
Spine/Paraspinal Sarcoma: Clinical Trial

- **Radiation Therapy**
- **CTV1 (clinical target volume)**
  - Tissues suspected of microscopic involvement
  - Doses: 50.4 GyE at 1.8 Gy per fraction
    - Could be given with photons
    - Majority of pts received ~30.6 Gy with photons (conformal or IMRT)
  - Treated pre-operatively when possible to doses of:
    - 19.8 Gy: Sacrum
    - 45-50.4 Gy: Thoracolumbar spine
    - Reduces risk of tumor seeding into wound
    - Dose selection based upon risk of wound healing delay
    - CTV dose reduced to 45-46.8 Gy with diabetes, concurrent chemoRx
Spine/Paraspinal Sarcoma: Clinical Trial

• Radiation Therapy
  – CTV1 (clinical target volume)
    • Controlled information on extent of CTV1 not available
    • CTV1 based upon the patterns of failure in surgical and radiation therapy series
    • Generally included the entire involved vertebral body and at least hemi-sacral segment in the CTV1 and one level above and below
    • Areas of extra-osseous extension into soft tissue are included with 1-1.5 cm margin or to fascial barrier
    • Scar coverage for patients receiving post-op XRT dependent upon histology, grade, length of scar
Spine/Paraspinal Sarcoma: Clinical Trial

- **Radiation Therapy**
- **GTV (gross tumor volume)**
  - CTV2: Encompasses original gross tumor
    - Boosted to dose of 70.2 GyE at 1.8 GyE q.d. with protons
    - Giant cell tumor, Ewing’s sarcoma: 61.2 Gy
  - CTV3: Residual gross disease after surgery
    - Boosted to dose of 77.4 GyE at 1.8 GyE q.d. with protons
    - If IDDM or concurrent chemotherapy (i.e. osteosarcoma), doses reduced to 70.2-72.0 GyE
- **Chemotherapy**
  - Adriamycin not delivered concurrently
Spine/Paraspinal Sarcoma: CT myelogram for Radiation Planning

T6 spine/paraspinal Chondrosarcoma

CT myelogram for lesions above the conus to outline spinal cord
Spine/Paraspinal Sarcoma: Treatment Planning

• Target definition
  – MRI
  – CT (myelogram)
  – MRI/CT fusion
Sacral Chordoma

Treatment plan

S2-5 chordoma

Biopsy only

77.4 GyE (photons 30.6 Gy protons 46.8 GyE)

No evidence of progressive disease 32 months after start of proton treatment
Spine/Paraspinal Sarcoma: Set-Up Verification

Set-up Radiograph with Digitized Set-up Points, Actual (red) and Desired (blue) Isocenter Axes

Sacral Chondrosarcoma
Spine/Paraspinal Sarcoma: Treatment Planning

- **Normal tissue constraints**
- **Spinal cord**
  - Surface: 63 GyE  Center: 54 GyE (for length up to 5 cm)
- **Cauda equina**
  - Limit dose to contralateral nerves when possible
- **Rectum**
  - Use omental flap to displace rectum for sacral chordomas
- **Small bowel**
  - 50.4 GyE
- **Skin**
  - Avoid full dose on skin overlying sacrum
$^{90}$Y Plaque Irradiation

Plaque on Dura
Spine and Paraspinal Sarcoma

• Accrual: 50 Patients 12/1997-3/2005

• HISTOLOGY
  – Chordoma 29 Chondrosarcoma 14
  – Liposarcomas 1 Angiosarcoma 1
  – Ewing’s Sarcoma 1 Giant cell tumor 1
  – MPNST 1 Osteosarcoma 1
  – Spindle + round cell 1

• Thoracic 11 Lumbar 13 Sacrum 26

• Primary 36 Locally recurrent 14
Spine and Paraspinal Sarcoma

- Extent of surgery
  - Grossly resected 25
    - Margins (+) 17 Margins (-) 8
  - Subtotally excised 12
  - Biopsy only 13
    - Size 7 cm median (Range 3-20 cm)

- XRT Median Dose 76.6 GyE (Range 59.4-77.4 GyE)
  - All but 1 patient completed Rx (social reasons)
  - Dose delivery within 3% of protocol target in all patients
    - Spinal cord dose constraint
  - Dural Plaques 3 patients
Spine and Paraspinal Sarcoma

• Results
  – Median follow-up: 34 months (living patients)
  – Local Recurrence: 6 at 8-43 months after start of XRT
    • 4 Isolated 2 also with distant metastases

  • 2/29 Chordomas 4/14 chondrosarcomas* p=0.016
  • 4/14 locally recurrent tumor vs. 2/36 for primary tumor, p=0.013

* Two patients had 4-5 prior recurrences and another had a dedifferentiated chondrosarcoma with tumor cut-through.
Spine and Paraspinal Sarcoma

• Local Failure  All Patients (n=50)
  – R0  0/8
  – R1  2/17  R0 vs. others  p= 0.028 (1-sided)
  – R2  3/12  p= 0.028 (1-sided)
  – Biopsy only 1/13  p=0.107 (2 sided)

• Local Failure  Chordoma (n=29)
  – R0  0/7  R0 vs. others  p= 0.149 (1-sided)
  – R1  1/10  p= 0.314 (2 sided)
  – R2  0/3
  – Biopsy only 1/9  p=0.314 (2 sided)
Spine and Paraspinal Sarcoma

• Metastases
  – Isolated distant metastases: 4 at 10-35 m after XRT

• Survival
  – 4 tumor deaths
    • 2 chondrosarcoma, 1 chordoma, 1 MPNST
  – 2 died unrelated causes
    • Cardiac, Oral cancer
  – 1 lost to follow-up
Local Control from RT Start (months)

0% 20% 40% 60% 80% 100%

0 12 24 36 48 60 72 84 96 108
Spine and Paraspinal Sarcoma

• Acute Complications
  – > Grade 3
    • 1 sacral insufficiency stress fracture after fall following surgery and 27 Gy without late sequelae.

• Late Complications
  – > Grade 3
    • 2 sacral neuropathies: Unresected sacral chordomas (77.4 GyE)
      – L leg weakness, stress urinary incontinence, ↓ rectal tone (5.5 y)
      – 1 erectile dysfunction at 4 yrs not responsive to sildenafil
    • 1 sacral insuff Fx after fall after S + 77.4 GyE → nail; chronic pain
    • 1 Rectal bleeding: Resected sacral chordoma+70.2 GyE at 2 years
  – Grade 2
    • 1 erectile dysfunction: 46 y.o. recurrent T3-5 chondrosarcoma and cord compressions (77.4 GyE) at 2 years; responsive to sildenafil
Spine and Paraspinal Sarcoma

• Conclusions
  – High dose photon/proton XRT can be delivered
  – Morbidity to date appears acceptable.
  – Encouraged to date by the treatment results with these challenging tumors
    • Await further follow-up, especially for the chordomas
    • Prefer to radiate at time of initial presentation
  – Potential concern about late sacral nerve toxicity in patients receiving 77.4 Gy
Axial Osteosarcomas

- Osteosarcomas of spine, pelvis, skull
  - Satisfactory resections difficult
  - Local failure more common

- Cooperative Osteosarcoma Study Group
  - Pelvic lesions: Local failure 70%
    - Resected 62%; Unresected 94%
    - 5 Yr EFS: 14% ; OS 28.9%
  - Spine lesions: Local failure 68%
    - 3/22 (13.6%) Disease Free at 6 years
    - OS better with XRT after intralesional Surgery or Bx

- Meta-analysis: Head and neck lesions
  - Local failure ~50%
Chemoradiation Therapy for the Treatment of Osteosarcoma

- Machak et al (Moscow)
  - 31 extremity sarcoma pts
    - Refused amputation after chemotherapy
    - Actuarial local control at 5 years: 56%
  - 11 patients had good imaging/biochemical response
    - Local control 100%  Survival 90%
Unresectable Sacral Osteosarcoma

Coronal T1 post-gadolinium MRI
19 year old with S1 Osteosarcoma

Initial progression after cisplatin/adriamycin and MTX

Responded to ifosfamide/etoposide

Concurrent chemoradiation with ifosfamide/etoposide starting week 16

70.2 CGE (photons 18 Gy protons 52.2 CGE)
Unresectable Sacral Osteosarcoma

Treatment Plan (Axial)

19 year old with S1 Osteosarcoma

After 12 weeks of chemotherapy

Concurrent chemoradiation starting week 16

70.2 CGE (photons 18 Gy protons 52.2 CGE)
Unresectable Sacral Osteosarcoma

Axial CT scan
19 year old with S1 Osteosarcoma

16 months after treatment

Chemotherapy +
70.2 CGE (photons 18 Gy
protons 52.2 CGE)

No evidence of progressive disease
at 4 years after treatment
Sacral Chordoma

T1 post-gadolinium sagittal MRI

Pre-treatment

S3-4 chordoma

77.4 GyE (photons 30.6 Gy protons 46.8 GyE)
Sacral Chordoma

Treatment Plan

S3-4 chordoma

Biopsy only

77.4 GyE (photons 30.6 Gy protons 46.8 GyE)
Sacral Chordoma

T1 post-gadolinium sagittal MRI

S3-4 chordoma

Biopsy only

77.4 GyE (photons 30.6 Gy
protons 46.8 GyE)

No evidence of progressive disease
at 36 months
Chordomas of the Sacrum

• Schoenthaler *et al.* (Lawrence Berkeley Lab) 1977-1989
  – Charged particles helium and neon
    • 14 pts sacral chordoma: Post-op XRT
      – 10 patients have gross residual disease
      – Median dose 75.65 CGE
      – Local control 55% at 5 years
  • Trend to improved LC
    – Neon vs. helium (62% vs. 34%)
    – Complete vs. partial resection (75% vs. 40%)
    – Treatment under 73 days (61 vs 21%)
Chordomas of the Sacrum

• Schoenthaler et al. (Lawrence Berkeley Lab)
  – Complications
    • No neurologic sequelae or pain syndromes.
    • One previously irradiated patient required colostomy.
    • One delayed wound healing after (-) post-RT biopsy.
    • One second malignancy.
    • There were no genitourinary complications.
  – On the basis of that experience, the investigators felt that additional evaluation of heavier charged particles was warranted.
Sacral chordoma treated with carbon ion 70.4 GyE/16 Fx

Courtesy of Tadashi Kamada, M.D., Ph.D.
Carbon Ion Therapy

• Carbon ions are under study in Japan and Germany
• Less lateral diffusion and sharper Bragg peak
• Higher RBE (~3) that may be even higher in tumor vs. normal tissue because of
  • Lower oxygen enhancement ratio (OER)
    – ? Relatively more effective vs photons against hypoxic tumor
  • ↓ capacity for sublethal/potentially lethal damage repair
    – ? More effective against slowly proliferating tumors
• Cost is higher than protons
  – Hyogo (2001: 28 B ¥/ $ 230 million) vs. ~ $100 million proton
  – Will be important to define indications for carbon ions
Carbon Ion Therapy for Bone and Soft Tissue Sarcomas

• Kamada et al. (NIRS, Chiba, Japan)
  – Phase I/II Study of Carbon ions 1996-1999
  • 57 patients with 64 sites of unresected sarcomas
    – Pelvis: 32 patients
    – Spine/paraspinal: 19 patients
    – Extremities: 6 patients
  • Total dose: 52.8-73.6 carbon GyE in 16 fx of 3.3-4.6 GyE over 4 weeks
Carbon Ion Therapy for Bone and Soft Tissue Sarcomas

• Kamada *et al.* (NIRS, Chiba, Japan)
  – 7/17 patients treated with 73.6 GyE developed RTOG grade 3 acute skin reactions.
  • Dose escalation was then halted at this level.
  – No other severe acute reactions (grade > 3)
  – Local control rate of 73% at 3 years
  – Overall survival rate of 46% at 3 years
  – Further studies at 70.4 GyE/16 fx of 4.4 GyE
Carbon Ion Therapy for Bone and Soft Tissue Sarcomas
Carbon Ion Therapy for Bone and Soft Tissue Sarcomas

Local Control

Dose 64-73.6GyE
Log-Rank (p=0.035)

Dose 52.8-57.6GyE
Chordomas of the Sacrum

• Imai et al. (NIRS, Chiba, Japan)
  – 30 patients with unresectable sacral chordomas
    • 23 primary 7 local recurrent after resection
      – Clinical target volume 546 cm³
    • 52.8-73.6 GyE (median 70.4) in 16 fx over 4 weeks
  – Local control rate at 5 years: 96%
    • 26 patients alive
    • 24 disease-free at median f/u of 30 months (range, 9-87 mos)
  – Two skin/soft tissue complications requiring skin grafts.
  – No other treatment-related surgical interventions, including colostomy or urinary diversion, were carried out.
  – All patients have remained ambulatory and able to stay at home after carbon ion radiotherapy
Chordomas of the Sacrum

- Imai et al. (NIRS, Chiba, Japan)
Carbon-Ion Therapy for Skull Base Chondrosarcomas and Chordomas

Schulz-Ernter D, Debus et al. IJROBP 2004

87 patients, 1997-2002, F/U: 3-54 months, median 20 months, Median dose 60 CGE (60-70 CGE) in 20 fractions

Chordoma Local Control: 81% at 3 years
Ewing’s Sarcoma

• Isaacson et al (Stockholm, Sweden)
  – Compared conformal treatment plans with photons and protons for a spinal Ewing sarcoma.
  – Even when only the final 20% of the treatment, the boost to the gross disease, was given with protons, they noted a 5% improvement in local control for a comparable predicted risk of spinal cord injury

• *Radiother Oncol* 1997;45:63-70.
Paravertebral Epithelioid Sarcoma
Intensity Modulated Protons (IMPT) vs. Intensity Modulated Photons (IMRT) (7 field)
Pelvic Bone Sarcomas

• Surgical morbidity can be high for lesions involving the acetabulum
  – Hoffman et al. (Munster, Germany)
    • Hindquarter amputation
      – 0/8 able to ambulate in the community
    • Endoprosthetic replacement had better function
      – 4/10 able to ambulate in the community (p=0.015)
  • While these patients were able to adapt well to their new living conditions, significant interventions were necessary for them to deal with problems such as restricted mobility or changing jobs or job orientation
Pelvic Chondrosarcoma

Managed by curettage, autografted bone, and protons 74 GyE in 37 fx
Pelvic Chondrosarcoma

No evidence of progressive disease at 36 months. Two other cases 14-36 months after treatment.
Protons: Soft Tissue Sarcomas

- SITES WITH POTENTIAL BENEFIT
  - Retroperitoneum
    - Reduce dose to bowel, other viscera
  - Trunk
    - Reduce dose to lungs, heart, viscera
  - Extremities
    - Reduce dose to joints, bone, gonads, anus
Retroperitoneal Sarcomas

• ~ 15% of soft tissue sarcomas occur in the retroperitoneum
• Primary management is attempt at complete surgical resection
• High rates of local recurrence
  – Following complete resection, 44-59% local recurrence rates at 5 years
    • Ultimate local failure rate may be > 70%
    • Contrast with extremity where local failures < 10%
• Wide surgical margins are difficult to achieve because of proximity of critical normal tissues
  • Liver, stomach, small bowel, kidneys, aorta, vena cava, mesenteric vessels, lumbosacral nerves
Retroperitoneal Sarcoma

51 year old female with grade 2/3 spindle cell sarcoma of the right retroperitoneum
Retroperitoneal Sarcomas

- Radiation therapy is clearly an effective local adjuvant treatment for extremity sarcomas
  - Efficacy for retroperitoneal sarcomas less clear
  - US NCI trial
    - Post-op external beam 50-55 Gy vs. IORT 20 Gy + external beam 35-40 Gy
    - Lower local recurrence rates with IORT 6/15 (40%) vs. 16/20 (80%) with external beam
      - Less enteritis (2/15) with IORT vs. 10/20 with external beam
      - More neuropathy (9/15) with IORT versus 1/20 with external RT
    - ACOSOG randomized trial of surgery vs. pre-op XRT failed
  - External beam doses traditionally limited to 45-50 Gy
Retroperitoneal Sarcoma

IMRT

– Dose delivery superior to 3D-CRT
– Musat et al (Institute Bergonie)
  • Rx planning study to ↑ dose from 45 Gy with 3D-CRT to 54 Gy using 5 theoretical IMRT plans using the case of patient given post-op XRT via 3D-CRT
  • Improvement in dose homogeneity of 2%-6%
    – Improvement in coverage factor (CF) by 9-16%
    – Improvement in dose to OAR by 11%-24%
    – Improved conformity index (CF x PF) 15-32%
  • IMRT should permit dose escalation without increasing dose to OAR
A COMPARISON OF 3D CONFORMAL PROTON THERAPY, IMPT, AND IMRT FOR RETROPERITONEAL SARCOMA


ASTRO 2006
24 year old with Liposarcoma

3D Proton

IMXT

IMPT

Harvard Medical School
Protons, IMPT, or IMRT for Retroperitoneal Sarcomas

- Largest treatment planning study for retroperitoneal sarcomas.
- IMPT, 3D CPT, and IMXT provide excellent target coverage within normal tissue constraints to doses of 50.4 Gy.
- IMPT and IMXT plans result in higher inhomogeneity within the target, but all techniques yield clinically acceptable outcomes.
Protons, IMPT, or IMRT for Retroperitoneal Sarcomas

- IMPT achieves the closest conformity.
- IMPT and 3D CPT provide the lowest radiation dose to OAR.
- Selective dose escalation to retroperitoneal margins of tumors achievable with IMPT.
Retroperitoneal Sarcoma

Selective Target Irradiation

• Recent report of selective pre-op XRT
  50 Gy of portion of the tumor

• 18 pts in whom pre-op CTV was just
  portion of tumor abutting posterior
  abdominal wall + 3 cm

  • All 18 patients were resectable
  • At median follow-up of 18 months, 1 local and 1
distant recurrence
    – Bossi et al (Leuven), ASTRO 2005
Retroperitoneal Sarcoma Boost
IORT: Retroperitoneum

5 year LC 74% and OS 83% in 16 pts after resection, 45 Gy pre-op XRT, and IORT (10-20 Gy)

Gieschen HL...... Willett CG.
IJROBP 2001;50:27.
3-D Conformal Radiotherapy

Pre-operative irradiation plan for a patient with a large, deep posterior leg soft tissue sarcoma.
Recent dosimetric studies have compared IMRT and conformal radiotherapy for STS sarcomas arising in the extremities, pelvis, trunk, and paranasal sinuses.

- IMRT plans were more conformal.
- In the extremities, bone and subcutaneous doses were reduced by up to 20%.
59 year old female with high grade posterior, proximal thigh sarcoma. IMRT used to spare vulva and femur. Note dose “bath”.
Protons: Trunk/Extremity Sarcomas

38 year with G2/3T1bN0M0 alveolar soft part sarcoma of the right shoulder.
Protons: Extremity

39 year old with high grade STS of thigh undergoing pre-op chemotherapy and XRT
Multiply Recurrent Desmoid Tumor after prior surgeries in dominant right forearm of a 50 year-old woman treated with shrinking field technique to 58 CGE with protons

A comparison between a photon (left) and a proton plan (right, treated).

Photon plan irradiate the entire circumference of the forearm.

Patient is now 2.5 years out from completion of treatment with local control, marked ↓ in pain, and no edema or late effects related to her RT.
Orbital Rhabdomyosarcoma

Courtesy T. Yock, N. Tarbell, J. Adams

Harvard Medical School

Photon  Proton