Osteosarcoma: The Past, Present and Future

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Disclosure

• Medical Board of Trustees for Musculoskeletal Transplant Foundation (MTF)
Objectives

• Discuss the advances in treatment and imaging of orthopaedic oncology that allowed limb-salvage surgery
• Compare historical options for reconstruction of the knee
• Understand current and future trends in reconstruction about the knee
Introduction

• 2800 cases/year in the United States of primary sarcoma of bone
  – Osteosarcoma
  – Chondrosarcoma
  – Ewing’s
  – Other (MFH, fibrosarcoma)
Anatomic Location

- Distal femur
- Proximal tibia
- Proximal humerus
- Proximal femur
Osteosarcoma in 2012
Osteosarcoma in 1966
McKenna, Schwinn, Soong, & Higinbotham, 1966
Development of Chemotherapy

• Around 1970 medical oncologists began using chemotherapy to treat osteosarcoma
Improvement in Imaging

- 1960’s and 1970’s saw widespread use of angiogram for visualizing soft tissues
- 1970’s saw use of CT scans, although resolution was still limited
“Local En Bloc Resection for Limb Preservation”

- 10 Patients received 4-8 weekly doses of methotrexate, citrovorum factor rescue, and vincristine
- 5 patients also received intra-arterial adriamycin
- Tx based on response by angiography
  - Responders (8/10) received limb salvage
  - Non-responders (1/10) amputated
  - One patient amputated secondary to complication from intra-arterial adriamycin
Choices for Reconstruction

- None (Amputation)
  - Modified amputation (Rotationplasty)
- Arthrodesis
- Arthroplasty
Surgical Reconstruction of the Skeleton Following Segmental Resection for Bone Tumors

By Philip D. Wilson, M.D.*, and Eugene M. Lance, M.D.*, New York, N.Y.

An Instructional Course Lecture, The American Academy of Orthopaedic Surgeons

A bone tumor confronts the orthopaedic surgeon with two problems: the cure of the disease and the preservation of maximum function in the affected part. The first consideration should almost invariably take precedence, and the decision to treat a lesion by segmental resection must be based on exact information about its nature and prognosis.

For instance, when a tumor, such as an osteogenic sarcoma, is highly malignant and metastasizing, amputation after necrotizing irradiation is the treatment of choice. However, in such primary malignant or close-to-malignant bone tumors as
Wilson & Lance, 1965

Surgical Reconstruction of the Skeleton Following Segmental Resection for Bone Tumors

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Various and creative use of autograft and allograft bone
Enneking & Shirley, 1977

- Twenty patients with tumors in the proximal tibia or distal femur treated by local resection and arthrodesis using an intramedullary rod and autograft
- One local recurrence
- “In properly selected patients, the method provided a stable extremity that permitted resumption of a vigorous life-style within approximately one year”
Enneking & Shirley, 1977
Enneking & Shirley, 1977
Enneking, Eady, & Burchardt, 1980

- 40 patients underwent resection of tumor with reconstruction by autogenous arthrodesis
- Union occurred in 67% (27/40) without an additional procedure by 20 months
- Fatigue failures or stress fractures occurred in 45% (18/40)
  - 72% (13/18) healed with conservative management
- Other complications
  - Hardware failure in 13% (5/40)
  - Infection in 13% (4 superficial, 1 deep)
  - Peroneal nerve palsy in 2 (1 resolved)
Enneking, Eady, & Burchardt, 1980

- Results
  - 30 good or excellent results
  - 7 fair
  - 3 poor
- “The term excellent is not meant to infer that a fused joint is the equivalent of a normal, moving, painless joint, but rather that the function, when judged as a result of fusion, is all that could be expected.”
Wolf, Scarborough, & Enneking, 1999

- 73 patients underwent resection, arthrodesis with use of autogenous grafts (10-yr f/u on 40 patients)
- Acknowledge a high complication rate
- Independent ambulation achieved in 86%
- MSTS scores in 32 patients at a mean of 17 years showed majority functioning satisfactorily
- “Resection arthrodesis using massive autogenous grafts should continue to be in the armamentarium of the orthopaedic oncologist.”
30 years earlier
Mankin, Fogelson, Thrasher, & Jaffer, 1976

- 19 patients underwent resection and allograft reconstruction (15 followed for a minimum of 6 months)
  - 12/15 healed host-graft junction without additional procedures
  - Other complications (16): hepatitis (2), infection (2), nerve palsy (2), ligamentous laxity (2), malunion, artery laceration, et al

- “Allograft replacement may in the future serve as an important approach to certain neoplastic conditions of bones and joints.”
Mankin, Doppelt, Sullivan, & Tomford, 1982

- 106 patients treated with resection and replacement with cadaveric allograft
  - 61 followed for >2 years
    - 45 osteoarticular
    - 10 intercalary
    - 6 allograft-prosthetic composite
Mankin, Doppelt, Sullivan, & Tomford, 1982

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- Total failure rate 16 %
  - 8% (5/61) recurrence or mets
  - 8% (5/61) amputated or implant removed for infection
- 74% (37/61) excellent or good
- 10% (6/61) fair
- Complications
  - Infection 13%
  - Pathologic fracture 10%
Results by implant type
- Osteoarticular allografts rated good or excellent – 67%
- Intercalary – 100%
- Allograft-prosthetic composite – 83%
Mankin, Doppelt, Sullivan, & Tomford, 1982

• “In long-term follow-up, the data suggest that if no complications ensue in the first two years, the results are generally quite good and the grafts show no evidence of progressive deterioration with time.”
Gebhardt, Flugstad, Springfield, & Mankin, 1991

- 53 patients with high-grade osteosarcoma treated with wide resection and allograft reconstruction
  - Osteoarticular allograft (19)
  - Intercalary allograft (2)
  - Allograft-prosthetic composite (10)
  - Allograft arthrodesis (22)
- 38 patients followed for ≥ 2 yrs.
Gebhardt, Flugstad, Springfield, & Mankin, 1991

- Complications
  - 16 infections
  - 6 fractures
  - 12 nonunions
  - 6 unstable joints
- 34% (18/53) grafts failed necessitating 6 (11%) AKA

- Functional “end-results” of 38 patients with ≥ 2 yrs f/u was 70% satisfactory in those without a local recurrence
• “The functional results are comparable to other methods of reconstruction, and once incorporated by the host, offer the advantage of longevity, compared with metallic implants.”
Rosen, Murphy, Huvos, Gutierrez, & Marcove, 1976

- 20 patients with biopsy proven osteosarcoma of distal femur or proximal tibia evaluated for chemotherapy and surgery
- CXR
  - Chest tomography
  - Skeletal survey
  - Bone scan
  - Femoral arteriogram
  - Full length scanogram of both lower extremities
Based on measurements from scanogram a custom prosthesis is ordered.

While patient awaits prosthesis, they are started on chemotherapy
  – High dose methotrexate
  – Citrovorum factor rescue
  – Adriamycin
Rosen, Murphy, Huvos, Gutierrez, & Marcove, 1976

- After 2-3 months of chemotherapy patient underwent complete resection of osteosarcoma and reconstruction with custom megaprosthesis
- 4-8 weeks post-operatively restarted on chemotherapy
- 15 patients who eventually underwent prosthetic replacement
  - 14 alive with no evidence of disease (NED) at 7-21 months (median 11 months)
  - 3 underwent AKA (infection 2, loss of sensation in foot/inability to walk 1)
Horowitz, Glasser, Lane, & Healey, 1993

- 93 patients underwent resection of lower extremity sarcoma and reconstruction with megaprosthesis
  - 16 proximal femur
  - 61 distal femur
  - 16 proximal tibia
- Minimum f/u 24 months, median of 66, mean of 80
Horowitz, Glasser, Lane, & Healey, 1993

• Event free prosthetic survival at 5 years
  – Proximal femur 88%
  – Distal femur 59%
  – Proximal tibia 54%
Horowitz, Glasser, Lane, & Healey, 1993

- Limb survival at 5 years
  - Proximal femur 88%
  - Distal femur 88%
  - Proximal tibia 78%
Horowitz, Glasser, Lane, & Healey, 1993

- Aseptic loosening survivorship at 5 yrs.
  - Proximal femur 100%
  - Distal femur 78%
  - Proximal tibia 73%
Horowitz, Glasser, Lane, & Healey, 1993

- Patient survival at 5 yrs.
  - Proximal femur 62%
  - Distal femur 75%
  - Proximal tibia 93%
Horowitz, Glasser, Lane, & Healey, 1993

• “Aseptic loosening in the locations of the distal femur and proximal tibia has become the most significant long-term problem. Approximately 25% of the prostheses in this location have become loose at five years.”
Muschler et al., 1995

- Between 1979 and 1986, 37 patients with sarcoma of distal femur underwent limb salvage with a custom megaprosthesis.
Muschler et al., 1995

• 35% (13/37) had early complications
  – 10 with skin necrosis
  – 3 infections
  – 3 DVT’s
  – 2 neurologic injuries
  – 1 with fat emboli
  – 1 with hematoma

• 38% (14/37) had late complications
  – 6 femoral aseptic loosening
  – 1 tibial aseptic loosening
  – 2 tibial fractures
  – 2 contractures
  – 1 femoral fracture
  – 1 prosthetic fracture
  – 1 septic loosening
| Enrollment was 1979-1986 | • 2-yr prosthetic survival was 82% |
| By 1988 | • 5-yr prosthetic survival was 57% |
| – 9 patients died | • 85% (22/26) had undergone successful limb salvage |
| – 13 prostheses failed in 12 patients | • Overall five year survival for patients with IIB osteosarcoma was 66% |
| • 9 revisions | |
Muschler et al., 1995

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Harrington, Johnston, Kaufer, Luck, & Moore, 1986

- 42 patients with sarcoma underwent resection, gross debridement of tumor tissue, autoclave resected bone and replace over intramedullary fixation (sometimes in conjunction with prosthetic reconstruction)
- Patients followed for a minimum of 2 years and 9 months
  - 28 with low-grade sarcoma
  - 14 with selected high-grade sarcoma
Harrington, Johnston, Kaufer, Luck, & Moore, 1986

- Tumor-related problems
  - 6 patients (all HG) developed recurrence (2) or metastases (4)
  - 0 patients w/ LG developed recurrence or mets

- 15 patients developed non-tumor related problems
  - 2 amputations for infection and pseudoarthrodesis
  - 1 infection underwent I&D
  - 6 revisions 2° mechanical failure or loosening
  - 5 non-unions required reoperation
It is not the purpose of this paper to suggest that the use of an autoclaved autogenous graft, usually in association with joint arthroplasty, necessarily is the best technique for limb reconstruction after tumor resection.

However, in appropriately selected individuals, the technique offers the surgeon the advantage of being able to use local bone for reconstruction, to preserve adjacent joint motion, and to allow immediate full weight-bearing after treatment.
Unique Challenges

• Resection of distal femur or proximal tibia in a young child will result in significant limb length discrepancy

• Even after limb salvage was being used for teenagers, amputation was still standard for kids <12 yrs
Kotz & Salzer, 1982

- 4 patients with distal femoral osteosarcoma underwent rotationplasty
- Followed for 27-58 months
- 1 patient died of mets
- 3 no evidence of recurrence and good functional results
- “Serious psychological problems” in both patients and parents in all cases
• Advocates use of rotationplasty in younger patient for whom no other alternative is reasonable
• Functional results in two patients was “remarkably good”
Lewis, 1986

- 6 patients with femoral or tibial resection for osteosarcoma (4) or Ewing’s sarcoma (2)
- Reconstructed with expandable megaprostheses
- 4 patients underwent 6 successful lengthenings
- F/u < 21 months
Eckardt et al., 2000

- Between 1984-1996 32 expandable prostheses were used for limb reconstruction after resection of bone sarcoma

- 22 Lewis Expandable Adjustable Prostheses (LEAP)
- 4 modular Wright Medical prostheses
- 4 modular Howmedica prostheses
- 2 Techmedica expandable prostheses
Eckardt et al., 2000

- Results
  - 12 patients died
  - 2 no evidence of disease
  - 17 continuously disease free

- 16 patients did not have an expansion
  - 10 w/ early death
  - 3 w/ early amputation
  - 3 were awaiting lengthening

- 16 patients underwent 32 lengthenings to a max of 9 cm
Eckardt et al., 2000

- Results continued
  - 14/32 patients had no complications
  - 18/32 patients had 27 complications

- Complications
  - 5 aseptic loosening
  - 4 collapse in LEAP prostheses
  - 4 temporary nerve palsy
  - 2 mechanical failure in LEAP prostheses
  - 2 fatigue fracture
  - 2 local recurrence
  - et al.
Eckardt et al., 2000

- Significant durability issue with any of the non-modular designs
- 8/22 (36%) ultimately failed and forced a revision of the design
Compress® Compliant Pre-stress Device

• High rate of failure of megaprostheses due to aseptic loosening
• Alternative means of fixation
Compress® Compliant Pre-stress Device

• Creates a stable, high-pressure bone-implant interface for biologic fixation, 1-3 and helps to prevent stress shielding

• Wolff’s Law – bone, when stressed, remodels to become stronger through dynamic bone compression
Compress® Compliant Pre-stress Device

- Creates a stable, high-pressure bone-implant interface for biologic fixation,1-3 and helps to prevent stress shielding
- Wolff’s Law – bone, when stressed, remodels to become stronger through dynamic bone compression
• In early human trial with Compress device one of the patients required amputation at 10 months
• Demonstrated a buttress of new bone
O'Donnell, 2009

- Retrospective review of 16 patients with resected tumors reconstructed with a megaprosthesis utilizing compressive osseointegration

- Average age 18 (12-42)
- Minimum f/u 2 yrs.
  - Mean 4.5
  - Range 2-10.3
O'Donnell, 2009

- Complications
  - 1 early deep infection (led to AKA)
  - 2 late deep infections (prostheses retained with I&D)
  - 1 developed aseptic loosening (required revision)

- Remaining 15 implants were stably fixed at last follow-up
Wunder, Leitch, Griffin, Davis, & Bell, 2001

- Comparison of the complications and functional outcome associated with the use of an APC or megaprosthesis after resection of a bone sarcoma from the distal femur or proximal tibia.

- Sequential cohort study
  - 11 received APC’s
  - 64 received tumor prostheses

- Primary measure was reconstructive failure (removal of the implant)

- Also measured function by MSTS rating system
Wunder, Leitch, Griffin, Davis, & Bell, 2001

- **Reconstructive failure**
  - APC’s 55% (6/11)
  - Mega’s 16% (10/64)
- **Reason for failure**
  - Infection
    - 18% (2/11) allografts
    - 6% (4/64) prostheses
  - Fracture (of allograft or prosthesis)
    - 36% (4/11) allografts
    - 8% (5/64) prostheses
  - Aseptic loosening
    - 1.5% (1/64) prostheses
Wunder, Leitch, Griffin, Davis, & Bell, 2001

- “Study suggests that limb salvage surgery at the knee has a better and more predictable outcome with a tumor prosthesis than with an allograft-implant reconstruction”
Holt, Christie, & Schwartz, 2009

- Trabecular metal implants used in reconstruction of 7 resections for bone sarcoma
- Age 13-71
- Minimum f/u 6 yrs
Holt, Christie, & Schwartz, 2009

• Results
  – 1 patient DOD
  – Average MSTS score 95%
  – No infection
  – No hardware failure
  – 1 implant failed because of loosening at 7 years
Holt, Christie, & Schwartz, 2009

• “In this small clinical series, the use of porous tantalum for limb salvage reconstruction is shown to be safe, to successfully provide osteointegration and soft tissue ingrowth, and to facilitate return of limb muscle function”
Where We’re Been

• Chemotherapy improved survival rates to 60-70% (this one’s on the oncologists)
• Better imaging and creative techniques improved limb salvage rates to 90% (this one’s on the surgeons)
Where We Are

- Amputation vs. arthrodesis vs. arthroplasty
- Autograft vs. allograft vs. metal
- Steady improvement in outcomes over the last 30 years
Current Controversies

• Proximal tibial resections: APC vs. megaprosthesis
• Method of fixation: cemented vs. uncemented
Where We’re Going

• Trabecular metal
• Compressive osseointegration
Case #1

- 15 y/o male presents w/ 5-6 wk. h/o right knee pain
- Biopsy confirms dx of osteosarcoma
- Staging reveals localized disease
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MRI

Axial T1+C

Axial T2
Restaging after neo-adjuvant chemo
Post-op Radiographs
Post-op Radiographs
Case #2

• 33 y/o female presents w/ 2-3 month h/o vague left knee pain
• Bx – c/w leiomyosarcoma of bone
• Remainder of staging studies negative
Case #2

- 33 y/o female presents w/ 2-3 month h/o vague left knee pain
- Bx – c/w leiomyosarcoma of bone
- Remainder of staging studies negative
MRI
Post-op Radiographs
References


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Thank You.