MSTS

ABSTRACT BOOK

September 27 – 29, 2017

Grand Hyatt Denver
Denver, Colorado

MUSCULOSKELETAL TUMOR SOCIETY

ANNUAL MEETING

2017

2017 MSTS Annual Meeting

Final Program

September 27 - 29, 2017
Grand Hyatt Denver
Denver, CO

Kevin A. Raskin, MD, Program Chair
Robert H. Quinn, MD, MSTS President

Educational Goals and Objectives

At the conclusion of this CME activity, the attendee should be able to:

Identify applications of limb-salvage surgery in non-oncologic patients.

Increase understanding of applications, limitations, and regulations of custom and 3-D printed prostheses.

Update recent progress in basic science research as it relates to musculoskeletal oncology.

Review and update the collaborate work being done and further identify future collaborative efforts for the society.

Address pain management for Orthopaedic Oncology patients in 2017.

Wednesday, September 27, 2017		
1:00 PM - 5:30 PM	Registration	
1:00 PM - 5:00 PM	Poster Exhibit Set-up	
1:00PM - 5:00 PM	Technical Exhibit Set-up	
6:00 PM - 8:00 PM	Welcome Reception	
Thursday, September 28, 2017		
6:30 AM - 5:30 PM	Registration	
7:00 AM - 8:30 AM	Breakfast	Colorado Ballroom - 2nd Floor
7:00 AM - 5:30 PM	Poster/Technical Exhibits	
10:00 AM - 10:20 AM	Product Theater - Exactech, Inc.	Maroon Peak - 2nd floor
1:50 PM - 2:45 PM	MSTS Business Meeting - open to MSTS members only	
2:45 PM - 3:30 PM	Product Theater - Onkos Surgical, Inc.	Maroon Peak - 2nd floor
2:55 PM - 3:15 PM	Poster Viewing - Question & Answer	Colorado Ballroom - 2nd Floor
7:45 AM	Meeting Opening - Welcome	Kevin A. Raskin, MD and Robert H. Quinn, MD
Session I: Extremity Surgery: Endoprosthetics and Allografts		

Moderators: Kathleen Beebe, MD and Lee Rodney Leddy, MD			
8:00 AM - 8:07 AM	Paper 1	Cemented Versus Uncemented Endoprostheses Following Resection Of Sarcoma: A Meta-Analysis Of Implant Survival And Aseptic Loosening	Valdis Lelkes, MD
8:07 AM - 8:14 AM	Paper 2	The Value Of Constrained Cups To Prevent Instability After Pelvic And Proximal Femur Complex Tumor Surgery	Jan Lesensky, MD
8:14 AM - 8:21 AM	Paper 3	What Is The Incidence Of Acetabular Erosion Following Hemiarthroplasty Endoprosthetic Reconstruction Of The Proximal Femur And Does It Affect Outcome?	Matthew Thomas Houdek, MD
8:21 AM -8:28 AM	Paper 4	Long Term (>15 Year) Outcomes Of All-Polyethylene Tibial Components For Endoprosthetic Reconstructions Of The Femur	Nicholas M. Bernthal, MD
8:28 AM - 8:35 AM	Paper 5	Evaluation Of The Olecranon-Ulnar (Ou) Angle In Preoperative Planning Of Distal Humeral Replacement	Caleb Yeung, MD
8:35 AM - 9:00 AM		Moderated Discussion	
Session II: Extremity Surgery: Endoprosthetics and Allografts			
Moderators: Pietro Ruggieri, MD, PhD and Francis J. Hornicek, MD			
9:00 AM - 9:07 AM	Paper 6	Lower Limb Reconstruction For Primary Bone Tumors In Children	Patrick Francis Curran, MD, MS
9:07 AM - 9:14 AM	Paper 7	Vascular Graft Reattachment Of Extensor Mechanism Fixation In Proximal Tibial Endoprosthetic Reconstruction	Odion Binitie, MD
9:14 AM - 9:21 AM	Paper 8	Massive Allografts Reconstruction Restores More Bone Stock Than Endoprostheses After A Femoral Non-Oncologic Failure.	Jose Ignacio Albergo, MD

9:21 AM - 9:28 AM	Paper 9	The Reverse Reamed Intercalary Allograft: A Surgical Technique	Benjamin Wilke, MD
9:28 AM - 9:35 AM	Paper 10	Revitalization And Accelerated Structural Allograft Union In Femoral Intercalary Reconstructions With A Vascularized Periosteal Flap. A Preclinical Study.	Roberto Velez, MD, PhD
9:35 AM - 10:00 AM		Moderated Discussion	
10:00 AM - 10:20 AM		Product Theater - Exactech, Inc.	Maroon Peak - 2nd floor
10:00 AM - 10:30 AM	Break		Colorado Ballroom - 2nd Floor
Session III: Complications : Saving a Limb-Salvage			
Moderators: Eric R. Henderson, MD and Herrick Siegel, MD			
10:30 AM - 10:38 AM	Paper 11	The Long-Term Survival Of Mega-Endoprosthetic Reconstructions After Two-Stage Revision Surgery For Periprosthetic Joint Infection	Wylie Y. Lopez, MD
10:38 AM - 10:46 AM	Paper 12	One Stage Revision With Placement Of Local Antibiotic Carrier In The Treatment Of modular Oncologic Joint Reconstruction	Herrick Siegel, MD
10:46 AM - 10:54 AM	Paper 13	Treatment Of Chronic Prosthetic Joint Infection And Concomitant Lengthening In Revision Distal Femur Replacement After Large Tumor Resection: A Case Report	Ridhi Sachdev, BS
10:54 AM - 11:15 AM		Moderated Discussion	
11:15 AM - 11:23 AM	Paper 14	A Collaborative Research Survey For The Establishment Of The International Endoprosthesis Registry For Sarcoma Treatment (Interest) Study Group.	Roberto Velez, MD. PhD
11:23 AM - 11:31 AM	Paper 15	Is Malnutrition Associated With Postoperative Complications In Patients With Primary Bone Sarcomas?	Andrew Park, MD

10:31 AM - 11:38 AM	Paper 16	Bulk Allograft Is More Susceptible To Infection Than Is Stainless Steel Or Cancellous Allograft Using A Mouse Model Of Infection	Nicholas M. Bernthal, MD
11:38 AM - 12:00 PM		Moderated Discussion	
12:00 PM - 1:00 PM	Lunch		Colorado Ballroom - 2nd Floor
Session IV: Topic Soft Tissue Sarcoma			
Moderators: Ginger E. Holt, MD and Kenneth Gundle, MD			
1:00 PM - 1:07 PM	Paper 17	Soft Tissue Sarcoma And Time To Treatment: An Analysis Of The National Cancer Database	Gannon Curtis, MD
1:07 PM - 1:14 PM	Paper 18	Vacuum-Assisted Closure In Sarcoma Resection May Improve Wound Complication Rates In Proximal Lower Extremity Tumors Treated With Preoperative Radiation	Meena Bedi, MD
1:14 PM - 1:21 PM	Paper 19	Morbid Obesity Significantly Increases The Risk Of Postoperative Wound Complications Following Upper Extremity Limb Salvage Surgery	Matthew Thomas Houdek, MD
1:21 PM -1:28 PM	Paper 20	Does The Modality Of Radiation Therapy Used To Treat Liposarcomas Of The Extremities Impact The Outcome?	Andrew Park, MD
1:28 PM - 1:35 PM	Paper 21	Soft Tissue Sarcoma Of The Extremities: The Value Of Treatment At High-Volume Centers	Alexander Leandros Lazarides, MD
1:35 PM -1:50 PM		Moderated Discussion	
1:50 PM - 2:45 PM		MSTS Business Meeting - MSTS Members Only	
2:30 PM - 3:30 PM		Break	Colorado Ballroom - 2nd Floor
2:45 PM - 3:30 PM		Poster Viewing & Question Session	Colorado Ballroom - 2nd Floor
2:55 PM - 3:15 PM		Product Theater - Onkos Surgical, Inc.	Maroon Peak - 2nd floor

Session V: Metastatic Bone Disease: Surgical Management and Novel Ideas			
Moderators: Wakenda K. Tyler, MD, MPH and David S. Geller, MD			
3:30 PM - 3:37 PM	Paper 22	Surgical Management Of Femoral Metastases In The Era Of Biologics: A Shifting Paradigm	Christina J. Gutowski, MD
3:37 PM - 3:44 PM	Paper 23	Mid-Term Results Of Patients Treated With Porous Tantalum Acetabular Implants For Non-Primary Periacetabular Lesions	Matthew Thomas Houdek, MD
3:44 PM - 3:51 PM	Paper 24	What Are The Short Term Costs Associated With Endoprosthetic Reconstruction Versus Surgical Fixation Of Bone Metastases From Renal Cell Carcinoma?	Syed Mohammed Karim, MD
3:51 PM - 3:58 PM	Paper 25	Critical Analysis Of Prophylactic Stabilization For Osseous Metastatic Disease In Long Bones With Low Mirels Scores	Adam S. Levin, MD
3:58 PM - 4:05 PM	Paper 26	Clinical Characteristics Of Acral Metastases	Keith Aziz, MD
4:05 PM - 4:12 PM	Paper 27	Operative Treatment Of Non-Primary Tumors Of The Acetabulum: Is A New Classification System Needed?	Matthew Thomas Houdek, MD
4:12 PM - 4:30 PM		Moderated Discussion	
Session VI: Quality of Life and Outcomes after Musculoskeletal Tumor Surgery			
Moderators: Lawrence R. Menendez, MD and Scott Edward Porter, MD			
4:30 PM - 4:37 PM	Paper 28	The Impacts Of Diagnosis And Surgical Acuity On Patient-Reported Outcomes Using Promis In Operative Patients With Malignant And Benign Tumors As Compared To Orthopaedic Trauma Patients And The U.S. Population.	Anna R Cooper, MD, MPH

4:37 PM - 4:44 PM	Paper 29	A Comparison Of Limb Salvage Versus Amputation For Non-Metastatic Sarcomas Using Promis Outcomes	Benjamin Wilke, MD
4:44 PM - 4:51 PM	Paper 30	Concurrent Validity And Responsiveness Of The Timed Up And Go Test (Tug) And The 10 Meter Walk Test (10Mwt) In Orthopaedic Oncology Patients	Alexandra K. Callan, MD
4:51 PM - 4:58 PM	Paper 31	Oncologic And Functional Outcomes Of Iliosacral Resection Without Reconstruction For Primary Bone Tumours	Kenneth Gundle, MD
4:58 PM - 5:05 PM	Paper 32	Results Of Promis Physical Functional And Pain Interference Scores In Surgically Treated Patients With Metastatic Bone Disease: Analysis After Early Patient Enrollment In A Multicenter, Prospective Study.	Alan Blank, MD, MS
5:05 PM - 5:20 PM		Moderated Discussion	
5:20 PM		Meeting Adjourns	
	Social Event - Underwater Adventure - Downtown Aquarium		
	6:00 PM & 6:15 PM	Buses Depart from Grand Hyatt Denver to Aquarium - two departure times	
	8:30 PM - 10:00 PM	Buses Return to Grand Hyatt Denver - Every 30 minutes beginning at 8:30 PM	
Friday, September 29, 2017			
6:30 AM- 8:30 AM	Registration		
7:00 AM - 8:30 AM	Breakfast	Colorado Ballroom - 2nd Floor	
7:00 AM - 11:00 AM	Poster/Technical Exhibits		
7:30 AM - 7:50 AM	Product Theater - Onkos Surgical, Inc.		
8:00 AM - 9:00 AM	President's Lecture - Speaker - Nicole Ehrhart, VMD, MS		
10:00 AM - 10:20 AM	Product Theater - Zimmer Biomet		
Session VII: AJCC Review for Orthopaedic Oncology & Basic Science Research			
Moderators: Justin E. Bird, MD and Peter S. Rose, MD			

9:00 AM - 9:14 AM	Paper 33	8th Edition AJCC Staging Manual Updates: Mini Symposia Changes to AJCC Bone and Sofe Tissue Sarcoma Staging	Jeffrey S Kneisl, MD
9:14 AM - 9:21 AM	Paper 34	Stability And Instability In Ewing Sarcoma: The Relationship Between Dna Repair And P53	Robert Carl Weinschenk, MD
9:21 AM - 9:28 AM	Paper 35	Oxygen Sensing By T Cells Establishes The Lung As An Immunologically Favorable Metastatic Niche	David Clever
9:28 AM - 9:35 AM	Paper 36	Osteoblast Inhibition Is A Novel Mechanism For Development Of Osteolytic Lesions In Renal Cell Bone Metastasis	Robert L Satcher Jr, MD
9:35 AM - 10:00 AM		Moderator Discussion	
10:00 AM - 10:20 AM		Product Theater - Zimmer Biomet	Maroon Peak - 2nd floor
10:00 AM - 10:30 AM		Break	Colorado Ballroom - 2nd Floor
Session VIII: Topic Basic Science/Research			
Moderators: Kurt Weiss, MD and Michelle Ghert, MD, FRCSC			
10:30 AM - 10:37 AM	Paper 37	Precision Medicine For The Treatment Of Osteosarcoma: Atrx Deficiency Predicts Enhanced Sensitivity To Rtrail	Julia Dawn Visgauss, MD
10:37 AM - 10:44 AM	Paper 38	The Most Cited Articles In Orthopaedic Oncology	Akash K. Shah, MD
10:44 AM - 10:51 AM	Paper 39	An Update On The Transcutaneous Osseointegration Experience In The United States	Rashmi Agarwal, MD
10:51 AM - 10:58 AM	Paper 40	Targeted Muscle Reinnervation: A Strategy To Prevent Neuroma And Phantom Limb Pain In Oncologic Amputees	John Alexander, MD
10:58 AM - 11:05 AM	Paper 41	F-18 Fdg Pet Differentiation Of Benign From Malignant Chondroid Neoplasms: A Systematic Review Of The Literature.	Juan Abelardo Augusto Pretell, MD
11:05 AM - 11:20 AM		Moderated Discussion	
Session IX: Topic New Ideas: Making " Impossible" - Possible			

Moderators: Nicola Fabbri, MD and Adam Linsday, MD			
11:20 AM - 11:27 AM	Paper 42	Management Of Recurrent Desmoid Fibromatosis Of The Upper Extremity	Erik T. Newman, MD
11:27 AM - 11:34 AM	Paper 43	"Is Surgery Justified In Aggressive Fibromatosis If We Are Supposed To Live Along With It?" Treatment Outcomes In 51 Patients	Harzem Orgzer, MD
11:34 AM - 11:41 AM	Paper 44	High Local Recurrence Rate For Giant Cell Tumor Of Bone After Neoadjuvant Denosumab Treatment	Yee-Cheen Doung, MD
11:41 AM - 11: 55 AM		Moderated Discussion	Aspen Ballroom - 2nd Floor
11:55 AM - 12:02 PM	Paper 45	A Comparison Of Outcome Of Treatment Paradigms For Sacral Chordoma: Does Preoperative Radiation Improve Prognosis?	Matthew Thomas Houdek, MD
12:02 PM - 12:09 PM	Paper 46	Clinical Outcomes Of Vascularized Fibular Graft For Treatment Of Late Radiation-Induced Complications In Long Bones	Mohamed Ahmed Yakoub, MD
12:09 PM - 12:16 PM	Paper 47	Computer-Assisted Surgery In Orthopedic Oncology. Indications And Results Of 164 Procedures.	Jose Ignacio Albergo, MD
12:16 PM - 12:30 PM		Moderated Discussion	Aspen Ballroom - 2nd Floor
12:30 PM - 1:00 PM	Discussant: Best Paper Award		
12:30 PM - 1:00 PM	Discussant: Best Poster Award		
1:00 PM	*Meeting Adjourns*		

Thank you for attending the 2017 MSTS Annual Meeting. Contact info@msts.org if you have any questions or additional comments you wish to share.

PAPER 1

Cemented versus Uncemented Endoprostheses Following Resection of Sarcoma: A Meta-Analysis of Implant Survival and Aseptic Loosening

Authors: Andrew Carbone, MD, Joseph A. Ippolito, MD, Alexander R. Willis, MD, Kathleen S. Beebe, MD, Joseph Benevenia, MD

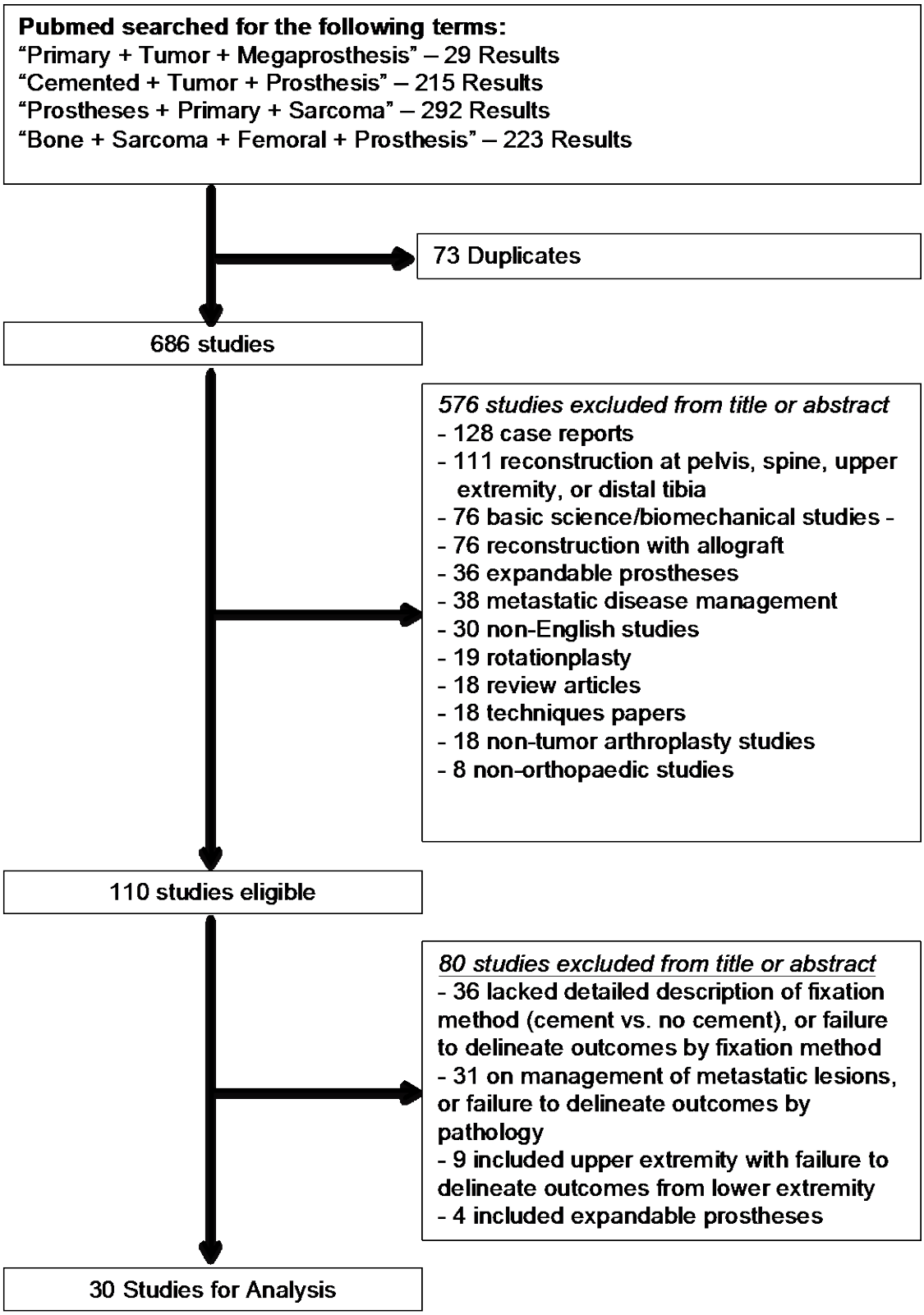
Background: Reconstruction with an endoprosthesis following resection of primary sarcomas of the proximal femur, distal femur, and proximal tibia have been widely published in the literature. Varying rates of complications, as well as mean functional outcome scores and long-term implant survival have been described.

Questions/Purposes: The objective of this analysis was to review previous reports on cemented and uncemented endoprostheses following primary sarcoma resection at the lower extremity and ask the following questions: (1) Do rates of aseptic loosening differ with versus without cementation of an endoprosthesis at the proximal femur, distal femur, or proximal tibia? (2) Does implant survival differ with versus without cementation of an endoprosthesis at the proximal femur, distal femur, or proximal tibia?

Methods: A primary literature search was performed in PubMed, which identified 686 studies related to reconstruction of the lower extremity with an endoprosthesis following resection of primary sarcoma. Inclusion criteria were patients with reconstruction with cemented or un-cemented endoprostheses following resection of primary bone sarcoma. Initial exclusion of studies (576) by review of abstracts left 110 full-length studies for detailed review. After review, 30 studies met inclusion criteria: 19/30 studies reported on cemented endoprostheses and 16/30 studies reported on uncemented prostheses. Meta Analysis was performed (using a fixed-effects model) using Odds Ratios (ORs) with 95% confidence intervals (95% CI) for binary outcomes of aseptic loosening and using Relative Risk (RR) with 95% CI for 2, 5, and 10-year non-oncologic survival rates.

Results: Overall, reported cemented versus un-cemented prosthesis survival was comparable at 2 years [86% vs. 87%; p=0.667], while greater survival was reported in cemented stems at 5-years [86% vs. 78%; p=0.0001]. Survival at 10 years was comparable between groups [69% vs. 33%; p=0.337]. Overall risk of aseptic loosening in cemented versus uncemented stems was comparable [13% vs. 12%; p=0.484]. Subgroup analysis of available data by anatomic location revealed increased risk of loosening with cement at the distal femur [12% vs. 8%; p=0.016], while risk was comparable at the proximal tibia [7% vs. 6%; p=0.528] and proximal femur [10% vs. 9%; p=0.727].

Conclusion: Reconstruction following resection of primary bone sarcoma is associated with considerable heterogeneity in patient age, diagnosis, defect size, and bone quality. Rates of aseptic loosening were higher at the distal femur with the use of a cemented endoprosthesis compared to an uncemented endoprosthesis, while overall prosthesis survival at 5-years was higher in cemented endoprostheses. Decisions for reconstruction must be based on each patient's unique disease characteristics and functional goals. Further prospective, randomized studies are warranted to elucidate underlying biomechanical differences between cemented and uncemented endoprostheses following resection of primary tumors, and identify areas for improvement in rates of aseptic loosening and overall prosthesis survival.



	Cemented	Uncemented	Significance
Implant Survival			
2 years	120/140 (85.7%)	179/205 (87.3%)	RR 0.98; 95% CI, 0.89-1.07; p=0.667
5 years	1452/1697 (85.5%)	599/765 (78.3%)	**RR 1.10; 95% CI, 1.05-1.14; p=0.0001**
10 years	1087/1561 (69.3%)	332/493 (32.7%)	RR 1.03; 95% CI, 0.97-1.11; p=0.337
Aseptic Loosening			
Overall	224/1724 (13.0%)	103/857 (12.0%)	OR 1.09; 95% CI, 0.85-1.41; p=0.484
Proximal Femur	44/433 (10.2%)	9/100 (9.0%)	OR 1.14; 95% CI 0.54-2.43; p=0.727
Distal Femur	80/680 (11.8%)	42/552 (7.6%)	**OR 1.6; 95% CI, 1.09-2.40; p=0.016**
Proximal Tibia	23/309 (7.4%)	8/138 (5.8%)	OR 1.3; 95% CI 0.57-3.00; p=0.528

PAPER 2

The Value of Constrained Cups to Prevent Instability After Pelvic and Proximal Femur Complex Tumor Surgery

Authors: Jan Lesensky, Patrick J. Boland, Daniel E. Prince, John H. Healey, Nicola Fabbri

Institutions: Orthopaedic Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, USA

Background: Instability is a common complication after complex hip reconstructive surgery. Common surgical scenarios are revision total hip arthroplasty and the management of primary and metastatic malignancies of the proximal femur and periacetabular region. In these circumstances, often characterized by lack of active and/or passive hip stabilizers, the mechanical lock of the hip joint by a constrained implant is an appealing option. However, failure of the locking mechanism, impingement, and early loosening requiring further surgery have been consistently reported after revision total hip replacement, raising concern about long-term outcome. Only few studies have investigated the use of constrained cups in oncologic patients with large periacetabular defects for primary or revision oncologic reconstruction or non-tumor massive bone loss.

Questions/Purposes:

1) Is a constrained cup design effective in preventing hip instability in a bone tumor setting?
2) Does this design allow early recovery and rehabilitation to a fully ambulatory status?
3) What is the incidence of complications and revision rate? What is the long-term implant survival?

Patients and Methods: This is a retrospective analysis of prospectively collected data. From 2007 to 2016, 47 patients (22 male, 25 female) with either bone sarcoma or metastatic cancer underwent primary or revision reconstructive surgery with the Biomet Freedom Constrained Acetabular Liner cup design.

The initial diagnosis was bone sarcoma in 21 patients, metastatic cancer to bone in 22 and a non-tumor massive defect in 4. Tumor was located in the pelvis in 27 cases and in the femur in 16 cases; all 4 non-tumor cases presented with a large periacetabular defect variably combined with femoral bone and soft tissue loss. Surgery consisted of primary reconstruction in 32 cases and revision in 15. Average age was 58 years. Seven patients were excluded because of death within 3 months from surgery. Forty patients (17 male, 23 female) were available for analysis at a median of 31 months' follow-up (range: 4-120 months). Twenty patients were alive at a median follow-up of 43 months, while 20 patients died after a median of 19 months). The end of follow-up was defined as the last office visit or contact, death, or removal of the implant.

Results:

1) The incidence of hip instability in this series was 5% (2 of 40 cases). One case was managed by closed reduction while the other was left unreduced. Both patients were terminally ill and died within 2 months from dislocation.
2) The rate of fully ambulatory status in this series was 98% (39 of 40 cases) at the index follow-up. One patient never recovered ambulation after surgery and died 7 months later. Eight patients needed an assistive device for ambulation while the rest walked without support.
3) Infection was the main postoperative complication with an incidence of 15% (6 of 40 cases). Of the 6 infected cases, 4 had a pelvic reconstruction. Implant revision was ultimately necessary in 4 of the 6 cases; 3 of these 4 patients had a pelvic reconstruction. The incidence of revision surgery for aseptic loosening was 20% (8 of 40) at median of 30 months. One patient suffered a femoral periprosthetic fracture at 36 months that was treated with open reduction and internal fixation.

Conclusions: The role of constrained cups in the surgical management of complex hip reconstructive is controversial. While intended to mechanically prevent dislocation, reported complications include a 30% rate of infection in the tumor setting and up to a 40-100% rate of subsequent failure after revision surgery for failed total hip replacement. We focused on a patient population exclusively represented by tumor and tumor-like cases involving the pelvis and/or proximal femur. This specific constrained cup design proved to reliably address stability and patients' return to ambulatory status. Infection and aseptic loosening were the most common complications, although the incidence was slightly lower than currently reported in the literature. As most of these patients had pelvic malignancies, a 15% infection rate appears acceptable, while a 20% rate of loosening at 30 months is much less satisfactory.
Patients with metastatic cancer and relatively short life expectancy may benefit most from constrained cup design, as it allows early recovery without the need for hip precautions. Risks and benefits should be carefully weighed in sarcoma patients with potentially long life expectancy, due to the high risk of aseptic failure. Given the retrospective design and the relatively small cohort in our study, we recommend future analysis of a larger population to provide sufficient power for comparison with revision surgery for total hip replacement.

PAPER 3

What is the Incidence of Acetabular Erosion Following Bipolar Endoprosthetic Replacement for Malignant Tumors of the Proximal Femur and Does It Affect Outcome?

Authors: Matthew T. Houdek MD, Peter S. Rose MD, Jay S. Wunder MD, Anthony M. Griffin MS, Franklin H. Sim MD, Peter C. Ferguson MD

Background: Endoprosthetic replacement is an option for reconstruction of the proximal femur to restore a functional extremity and achieve limb salvage. A bipolar component is typically used due to the concern for dislocation following these procedures, however due to the young age of these patients there is theoretical risk for degenerative changes of the acetabulum with long-term follow-up. Currently there is a paucity of data concerning the rate of degenerative changes of the acetabulum following these reconstructions and if it affects outcome.

Purpose: The purpose of this study was to examine a consecutive series of bipolar endoprosthetic replacements of the proximal femur performed for a malignant process to evaluate 1) overall patient and disease free survival, 2) rates of acetabular cartilage degeneration 3) rates of revision with a focus on conversion to total hip arthroplasty (THA) and 4) patient function.

Methods: A retrospective review of two large international tertiary sarcoma centers identified 148 consecutive patients who underwent a bipolar endoprosthesis following an oncological resection of a malignant tumor of the proximal femur over a 15-year period (2000-2014). Kaplan-Meier survival outcomes were assessed for overall survival and revision. Mean age was 57 years (range 11-89) at the time of the surgery with 54% being male. The most common pathology was metastatic disease (n=68, 45%). All surviving patients had 1-year follow-up with a mean follow-up of 6 yrs (1-15 yrs). The mean time to death was 2 yrs (range 1 day-15 yrs). Plain radiographs were used to assess for degenerative changes of the acetabulum as well as component migration. The Musculoskeletal Tumor Society (1993) rating was used to assess patient function.

Results: The mean 2-, 5-, 10-, and 15-year overall survival was 55%, 43%, 31% and 29%. In regards to survival of the implant, the 2-, 5-, 10-, and 15-year overall implant survival was 92%, 86%, 71% and 47%. Recurrent disease occurred in 29 patients (local n=4, local and distant n=2, and distant n=23). The mean time to revision 4 yrs. (range 2 weeks-15 yrs). Of these revisions, 12 patients were converted to a THA. Indications for conversion to THA included acetabular wear and pain (n=6), recurrent dislocations (n=4) and following reimplantation for infection

(n=2). Radiographic analysis showed the mean proximal migration of the bipolar component was 0.8 mm (range 0-20 mm). There was no difference in the proportion of patients with acetabular migration >2 mm who had undergone preoperative (OR 1.21, P=1.0) or postoperative (OR 1.34, *P*=0.72) radiotherapy or chemotherapy (OR 0.98, P=1.0). There was a significant difference in the mean follow-up of patients who developed acetabular wear (8±1.3 yrs vs. 4±0.5 yrs, P=0.0002). At last follow-up the mean MSTS rating was 56% (range 0-100%). There was no difference in the mean MSTS rating between patients who developed acetabular wear and those who did not (61% vs. 66%, P=0.44).

Conclusion: Following bipolar endoprosthetic replacement of the femur, there was an overall low rate of conversion to THA, with only 4% of patients undergoing conversion to THA due to groin pain and acetabular degeneration. Likewise, only a small percentage of patients (8%) developed visible radiographic changes of the acetabulum at final follow-up. As the length of follow-up increases however, a greater proportion of patients have visible radiographic changes. Although acetabular wear was present, it did not affect the functional outcome of patients at final follow-up.

PAPER 4

Long Term (>15 year) Outcomes of All-Polyethylene Tibial Components for Endoprosthetic Reconstructions of the Femur

Authors: Nicholas M Bernthal, Vishal Hegde, Stephen D Zoller, Howard Y Park, Zachary DC Burke, Gideon Blumstein, Jeffrey J Eckardt

Institution: University of California, Los Angeles Department of Orthopaedic Surgery

Background: Limb-salvage procedures utilizing endoprosthetic reconstruction after resection of primary bone tumors have been established as a standard of care for over three decades. All-polyethylene tibial (APT) components were one of the original tibial component designs used for both endoprosthetic reconstruction and TKA. Within the TKA literature there is continued debate about the durability of APT components when compared to their metal-backed tibia (MBT) counterparts. As the biomechanics of endoprosthetic reconstruction differ from standard TKA due to the existence of long bone segment defects, the TKA literature on APT components may not be directly applicable. In addition, the endoprosthetic APT literature is scarce and lacks long-term, high-quality clinical follow-up.

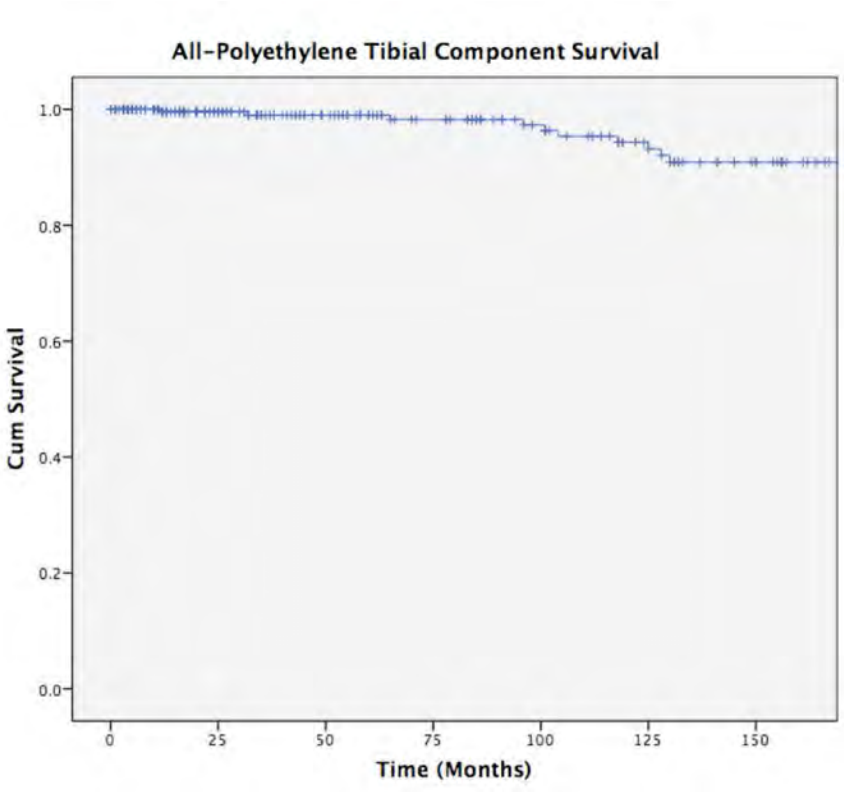
Purpose: We aim to examine the long-term survivorship and modes of failure of cemented APT components in endoprosthetic reconstruction. We also aim to examine the clinical outcomes of subsequent revisions due to the failure of a cemented APT component.

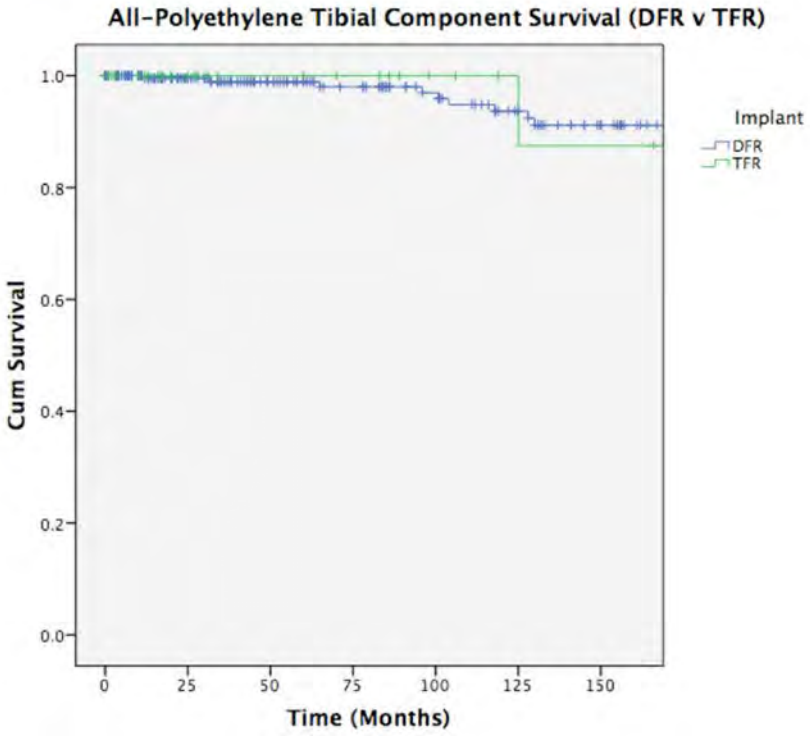
Patients and Methods: This is a retrospective review of our endoprosthesis database consisting of 512 consecutive cemented endoprosthetic reconstructions performed for oncologic diagnoses between 1980 and 2016. 277 of 512 (54.1%) of these were determined to be either distal femoral replacements (DFR) or total femoral replacements (TFR) utilizing an APT component. Bushing changes, revisions for adjacent joint pathology, and planned expansions of growing implants were excluded. Outcomes evaluated were APT component survival, revision surgery categorized according to the Henderson Failure Mode Classification, complications, and functional outcomes. Analyses were repeated for subsequent APT component revisions.

Results: Two hundred and seventy-seven patients (54.1%) underwent endoprosthetic reconstruction utilizing an APT component for either a DFR or TFR. Five-, 10-, and 15-year Kaplan-Meier survival of initial APT implants were 99.3%, 97.6%, and 96.2%, respectively. 15-year survival of APT components for DFR was 96.0%, and for TFR was 96.6%. Mean MSTS Score was 27 in this cohort. Of the 11 APT components that failed at 15-years, 6 failed due to aseptic loosening and 5 failed due to structural failure (mean 8.3 years post-op). Of those 11, 4 (36.4%) were revised to a MBT component, while 7

(63.6%) were revised to another APT component. One of the 7 (14.3%) revision APT components failed again (8.0 years post-op) and was revised to a MBT component.

Conclusion: At long-term follow-up, primary endoprosthetic reconstruction utilizing an APT component showed excellent 15-year survival (96.2%). The type of prosthesis (DFR v TFR) did not influence survival rates. In addition, outcome scores were high in this cohort. Considering that APT components are generally a lower-cost alternative to MBT components for endoprosthetic reconstruction, they provide a reliable option in the setting of a primary oncologic resection and ensuing reconstruction.





PAPER 5

Evaluation of the Olecranon-Ulnar (OU) Angle in Preoperative Planning of Distal Humeral Replacement

Authors: Caleb M. Yeung, M.D., Jonathan Lans, M.D., Zachary Wright, B.S., Connie Y. Chang, M.D., Santiago A. Lozano Calderon, M.D., PhD

Institutions: Orthopaedic Oncology Service, Department of Orthopaedic Surgery, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts

Background: The elbow is a challenging site for reconstruction following tumor resection in oncology patients and frequently requires reconstruction of the entire joint. The Solar Elbow System (SES) and the Modular Universal Tumor and Revision System (MUTARS) involve placement of an ulnar stem into the ulnar canal. Appropriate sizing of the ulnar stem component is crucial to prevent component cutout through the dorsal ulnar cortex. Unlike other joints, there is a lack of literature available regarding preoperative planning and osseous anatomy of the distal humerus and ulna. We describe the olecranon-ulnar (OU) angle, defined as the angle formed by the intersection of lines drawn parallel to the non-articulating outer cortex of the olecranon and the dorsal diaphyseal cortex of the ulna (Figure 1A), as a predictive factor for the size of the ulnar stem component. This will inform preoperative planning for ulnar component stem sizing to maximize component fit while limiting complications such as cortex perforation, periarticular fracture, or stem component failure.

Questions/Purpose: The first purpose of the study is to evaluate the normal variation of the OU angle in the general population. The second is to identify demographic predictors of the OU angle. The third is to identify the effect of the OU angle on the sizing of the ulnar stem component in SES and MUTARS templating.

Patients and Methods : Our study was IRB-approved and HIPAA-compliant. 526 normal and pseudonormal (non-native humerus/radius but native ulna without prior fracture or reconstruction) radiographs were retrospectively evaluated. The OU angle of each patient was measured by three independent observers twice each using ICIS PACS (Agfa), with >3 months elapsed between initial and repeat measurements. Patients were stratified into OU angle groups of <5°, 5-10°, and >10°; templating of MUTARS and SES was then performed using lateral elbow radiographs of 90 randomly selected patients (30 from each group). Calibration of radiographic images was done based on pixels/mm of the original radiograph. Templating was performed using the TraumaCad software system and modified to satisfy dimensions and locations (Figure 1B-D). The MUTARS has one size and a curved ulnar stem. The SES has three straight ulnar stem lengths (63mm, 53mm, and 50mm) and in small, standard and large sizes. There were two patients in which the large SES with a 63mm ulnar stem did not fit; therefore, we stratified the SES into two groups: (1) Large size and a 63mm stem, and (2) other smaller combinations. For statistical analyses, intrarater and interrater reliability was determined using

one-way and two-way random consistency analysis of Cronbach's alpha, respectively. Multivariate regression was used to determine the effects of age, gender, race, height, weight, and BMI on OU angle (Table 1A). Fisher's exact test and the Mann-Whitney U test were used to determine the impact of the OU angle on ulnar stem selection using the OU angle as a categorical and continuous variable, respectively. $p<0.05$ was considered significant for all tests.

Results: We show statistically strong interrater (Cronbach's alpha of 0.879) and intrarater reliability (Cronbach's alpha of 0.871, 0.918, and 0.935 for each rater). The median OU angle was 4.7^{o} with an interquartile range of 3.7^{o}. Multivariate regression analysis showed no significant prediction of OU angle by the age, gender, race, height, weight or BMI ($F(6, 508) = 2.704$, $p=0.01$, $R^2 = 0.02$). The MUTARS elbow implant fit in almost all elbows (96.7%) that had an OU angle of <5° and in 90% of the elbows with an OU angle ≥5° ($p=0.69$). The largest SES combination fit all elbows with an OU angle ≤10° compared to 28/30 of those with an angle of >10° ($p=0.33$). There was a trend towards smaller SES combinations when the OU angle was >10° using the angle as a continuous variable ($p=0.058$) (Table 1B).

Conclusions: Even robust preoperative review of lateral radiographs can result in overestimation of the minimal canal size of the ulna in selecting the ulnar component, predisposing to complications. We describe the OU angle as an important preoperative planning tool for distal humeral replacement. The OU angle is not predicted from common patient demographic data but must be defined on lateral elbow radiographs. Importantly, in patients with an OU angle of ≥5°, alternatives to the MUTARS should be made available as the curved ulnar stem may not fit. Production of several size selections for the curved ulnar stem may also be useful as straight ulnar stems are smaller in general, making them prone to loosening or stem fracture.

PAPER 6

Lower Limb Reconstruction For Primary Bone Tumors In Children

Authors: Patrick F. Curran MD, Richard J. O'Donnell MD, Rosanna L. Wustrack MD

Institution: Department of Orthopaedic Surgery, University of California, San Francisco

Background: The lower extremity is a common location for primary malignant tumors of the bone in children. Limb-salvage surgery has emerged as the standard of care over amputation for most patients with primary bone tumors. In children, limb-salvage surgery with fixed-length endoprosthesis can lead to limb length discrepancies. Many surgeons now use expandable implants to overcome this problem.

Purpose: The purpose of this study is to retrospectively compare outcomes of children who underwent resection of primary bone tumor and reconstruction with either static Compress® (SC) or expandable Compress® (EC) endoprostheses.

Patients and Methods: This study retrospectively reviewed all cases of limb reconstruction using compressive osseointegration in patients less than 18 years of age by a single surgeon at a single institution over an 18-year period. Primary outcomes included revision operation, limb salvage rates, and number of surgeries. Revision procedure was defined as any unplanned procedure, excluding limb lengthening or conversion of expandable to static prosthesis at skeletal maturity. Secondary outcome measures included implant outcomes: prosthetic joint infection, pathologic fracture, periprosthetic fracture, and oncologic outcomes: local recurrence, metastases, and patient death. Statistical analysis was performed with Student's t-test for continuous data and Chi-square for categorical data with significance set at $p < 0.05$. Survival of the implant and overall survival were determined using the Kaplan-Meier estimator.

Results: Fifty-eight pediatric patients (SC 38; EC 20) who underwent limb salvage surgery with an endoprosthesis with a minimum two-year follow up were included in this study. The mean age at limb-salvage procedure was significantly older for SC (14.4 ± 1.7 years) than EC (11.4 ± 2.3 years). There was no difference between the two groups by tumor type, tumor location, incidence of preoperative chemotherapy, and preoperative pathologic fracture. Thirty-two patients underwent reoperation (15 SC; 17 EC; $p < 0.05$) with 36 and 69 total procedures performed in the SC and EC groups, respectively. The rate of revision of primary implant was 34% for SC and 55% for EC at mean 5 years follow-up (Figure 1). The most common reasons for implant failure requiring revision surgery were infection and mechanical failure in the SC group and arthrofibrosis and mechanical failure in the EC group (Tables 1). Eight patients (40%) with EC endoprosthesis underwent lengthening procedures (Mean 2.4; Range: 1-8 procedures). Of patients who underwent revision, 5 SC (45.5%) and 1 EC (7.7%) underwent repeat revision surgery. The incidence of local disease recurrence, distant metastases, amputation, and mortality were similar between implant groups.

Conclusion: Static and expandable Compress® endoprostheses are viable limb-salvage reconstruction implants for pediatric patients. Expandable implants are associated with increased rates of complication and revision surgery, but allow for limb lengthening in skeletally immature patients. Despite the increased number of revision surgeries in the EC group, the infection rate was lower compared to the SC group and the overall limb salvage rate was higher.

Keywords: Bone tumor, Osteosarcoma, Limb-salvage

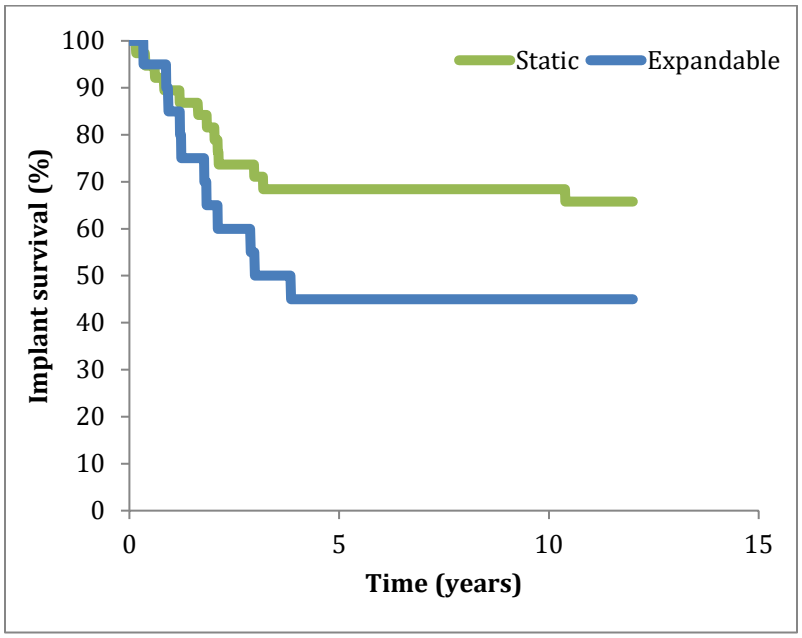


Figure 1: Kaplan-Meier curve for primary implant survival

		Static	Expandable
Mechanical		n (%)	n (%)
Type 1	**Soft-tissue failure**	2 (5.3)	18 (35)*†
Type 2	**Aseptic loosening**	1 (2.6)	1 (5)
Type 3	**Structural failure**		
	A – Implant	4 (10.5)	7 (20)*†
	B – Bone	1 (2.6)	0 (0)
Non-mechanical			
Type 4	**Infection**	8 (15.7)†	3 (15)
Type 5	**Local tumor progression**	1 (2.6)	1 (5)
Other			
	Distant metastases	12 (31.5)	8 (40)
	Death	8 (21.1)	6 (30)

Table 1: Henderson classification for total occurrence of each complication (% prevalence). *p < 0.05. † denotes multiple occurrences

PAPER 7

Vascular graft reattachment of Extensor Mechanism Fixation in Proximal Tibial Endoprosthetic Reconstruction

Authors: Amir Boubekri BSc, David Joyce, MD, G. Douglas Letson MD, Odion Binitie MD

Institution: H. Lee Moffitt Cancer Center, Tampa, FL

Background: Endoprosthetic reconstruction following the resection of proximal tibia bone tumors requires reattachment of the extensor mechanism. We sought to review surgical and functional outcomes in patients who underwent reconstruction utilizing a synthetic polytetrafluoroethylene tubular vascular graft to reattach the extensor mechanism to the endoprosthesis.

Purpose: 1) Do patients with a vascular graft reattachment have improved range of motion and reduced extensor lag? 2) Is there an increased risk of infectious complications in this group?

Methods: 47 consecutive patients who underwent a primary proximal tibial replacement at one institution from 1998-2016 were retrospectively reviewed. Mean age was 34 years (range 6-81) with 23 (49%) female and 24 (51%) male. The most common diagnosis was osteosarcoma (62%). 14 patients were excluded for less than one year follow-up, revision surgery, extra-articular resection, leaving a total of 33. 12 (37%) patients had a vascular graft for extensor mechanism fixation. All patients had a medial gastrocnemius muscle flap.

Results: Median follow-up for the 33 patients was 52 months (range 19-224). Median follow for the graft group was 27 months, non-graft 111 months. At last follow-up 19 patients were alive. There were a total of 12 revisions (36%). There were no extensor mechanism failures in the graft group, three in the non-graft group (p=.218). Extensor lag was improved in the graft group, mean 3º compared to 14º in the non-graft group (p=.108), mean flexion was 107º compared to 95º respectively (p=.15). Mean MSTS scores were similar in both groups 25 compared to 23 respectively.

Conclusion: Vascular graft usage for extensor mechanism fixation in proximal tibial endoprosthetic reconstruction provides a reliable technique for soft tissue fixation, reducing extensor mechanism failures, without an increase in infection.

PAPER 8

Massive allografts reconstruction restores more bone stock than endoprostheses after a femoral non-oncologic failure.

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Institution: Hospital Italiano de Buenos Aires. Argentina

Background: There are multiple types of reconstructions for the treatment of massive bone defects after an oncological resection. But, mainly they are divided into prosthetic or biological reconstructions. The placement of endoprostheses is technically simpler than a massive allograft and allows a faster postoperative recovery. However, these implants do not restore the secondary bone loss. Reconstruction with massive allografts requires a more demanding surgical technique and longer postoperative rehabilitation time, but the bone loss is supposedly restored after this reconstruction method. Therefore, it is assumed that in case of a reconstructive failure, endoprostheses produces a greater loss of bone capital than in the case of a failure of a massive allograft.

Questions/purposes: (1) To analyze the causes of failure of a massive allograft or a femoral endoprosthesis reconstruction; (2) to compare which of these reconstructions produces greater bone loss. (3) To determine how reconstructive failure was treated.

Methods: We retrospectively analyzed the records of patients treated with massive bone allografts or a modular endoprosthesis for a femoral bone tumor or as a femoral revision for a previous limb salvage procedure between 2000 and 2012. During this period, 201 patients were reconstructed with massive bone allografts and 107 endoprosthesis. Of the 201 allografts reconstructions, 50 (24%) had a non oncologic failure. Allograft failures were observed in 20 osteoarticular, 8 intercalary, 20 allograft-prosthetic composite reconstructions (APC) and 2 unicondilar allograft. Of the 107 femoral endoprosthesis, 16 (15%) had a non oncologic failure. Failures in this group include 15 distal femur reconstruction and 1 proximal femur endoprosthesis. Using chart and radiographic review, we measured bone stock, and determined 3 possible scenarios: 1- Loss of more than 2 cm of bone stock from the original resection osteotomy. 2- Loss of less than 2 cm of bone stock from the original resection osteotomy. 3- Increase of bone stock after reconstructive failure. No patient was lost to follow-up.

Results: In the allograft group, in 36 cases the failure was secondary to a fracture, 9 had a bacterial infection, 3 had a joint instability and 2 had an articular collapse. In the endoprosthetic group, in 10 cases the reconstruction failure was secondary to an infection, 5 had an aseptic loosening and 1 had a periprosthetic failure.

In the allograft group, all cases that failed due to fracture, joint instability or an articular collapse, increases bone sock after reconstructive failure. However, in patients who developed an infection, in 8 cases the bone loss was less than 2 cm and in one the bone loss was more than 2 cm from the original resection osteotomy.

All cases that had a failure of an endoprosthesis, suffered a bone loss of more than 2 cm from the original resection osteotomy.

In the allograft group (50 cases), 25 patients were converted to an endoprosthesis, 12 to an APC, 12 to a new massive allograft and one remained with a cement spacer until it died.

In the endoprosthesis group, 14 patients were converted to a new distal femur endoprosthesis, 1 to a total femur endoprosthesis and one remained with a cement spacer until last follow-up.

Conclusions: According to the results observed in this study, when an endoprosthesis reconstruction fails, there is a greater bone loss than is observed after a failure of a massive bone allograft. Therefore, we suggest considering the biological reconstruction that restores bone stock in young patients with a long life expectancy, in order to minimize the orthopedic complications that occur after loosening of tumor endoprosthesis.

PAPER 9

The Reverse Reamed Intercalary Allograft: A Surgical Technique

Authors: Benjamin Wilke MD, Anna Cooper MD, Parker Gibbs MD, Mark Scarborough MD, Andre Spiguel MD*

Institution: University of Florida Department of Orthopaedic Oncology. Gainesville, FL

Purpose: Allograft reconstruction of large segmental intercalary bone defects following tumor resection is a well-accepted surgical technique. Although results generally have been satisfactory, non-union at the allograft-host bone junction site remains a significant concern. We report an innovative reverse reaming technique that decreases the level of intraoperative difficulty mating the allograft-host junction and theoretically improves junctional healing by enhancing stability and increasing contact surface area.

Methods / Results: Following wide exposure, transverse osteotomies are created both proximal and distal to the tumor. The remaining host bone is then prepared using acetabular reamers to create a concave surface to dock the intercalary allograft. The allograft is then prepared on the back table. As the reaming will shorten the allograft it is advisable to cut the allograft approximately 1 centimeter longer than the measured defect and fine-tune the length through the reverse reaming process. We utilized the reverse reamer from the Equinox Shoulder Resurfacing system (Exactech, Gainesville, Fl). Both the proximal and distal ends of the allograft are reamed in this manner and the allograft is press-fit into position with excellent inherent stability. The convex-concave junction is intended to create a larger surface area at the allograft-host bone junction site in order to facilitate increased bridging bone as well as enhanced inherent stability compared to a transverse junction. Additionally, this allows for greater degrees of freedom in reducing the allograft to the host and is thus much more forgiving than either transverse or step cut osteotomies relative to alignment and fixation. In the tibia, with the fibula intact and soft tissue tensioned, there is enough stability and compression at the junctions to allow for fixation without much difficulty.

Once the allograft is in place, fixation is performed per the surgeon's discretion. We utilize a narrow 4.5 mm limited contact dynamic compression plates (LC-DCP) which can be contoured to fit the bone and secured in compression mode. Once the plate is secured to the host bone 2 to 3 locking screws can be placed into the allograft (depending on its size) to secure the construct. Bone graft obtained from reaming the patient's bone after the resection is then added around the junction sites. We attempt to save a sleeve of periosteum from the osteotomy sites in order to repair over the allograft-host bone junction in an effort to increase graft incorporation. Dual

plating may be used to increase construct stiffness with local muscle flaps as needed for wound coverage.

Conclusion:

The advantage of the reverse reamed intercalary allograft lies in the increased contact surface area between the host bone and the allograft, theoretically improving healing potential of the host-allograft junction. This improved contact area not only has the potential to improve junctional healing but also provides inherent stability during the reconstruction. It is simple to perform and allows rotational and slight angular corrections to be made once the allograft is in place. To our knowledge this is the first time this technique has been reported *in vivo*.

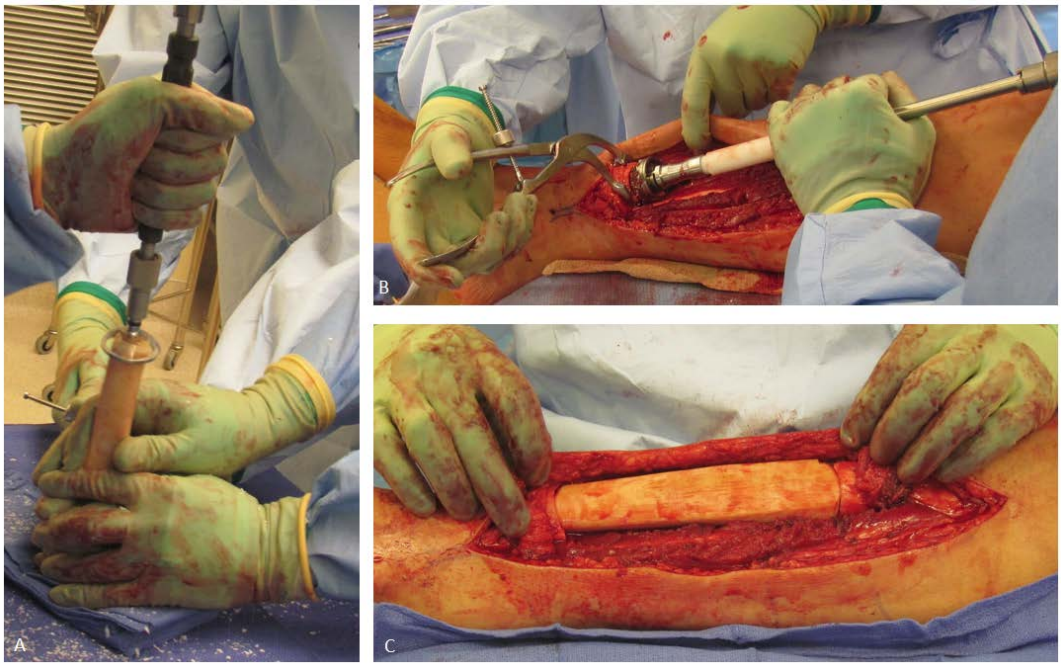


Figure 1a-c: The intercalary allograft is prepared on the back table with a reverse reamer (a). The ends of the host-bone tibia are reamed with a standard acetabular reamer, matching the diameter of the reverse reamer (b). The allograft press-fit into place (c). The allograft has excellent inherent stability, due to the increased contact surface area at the allograft – host bone junctions.

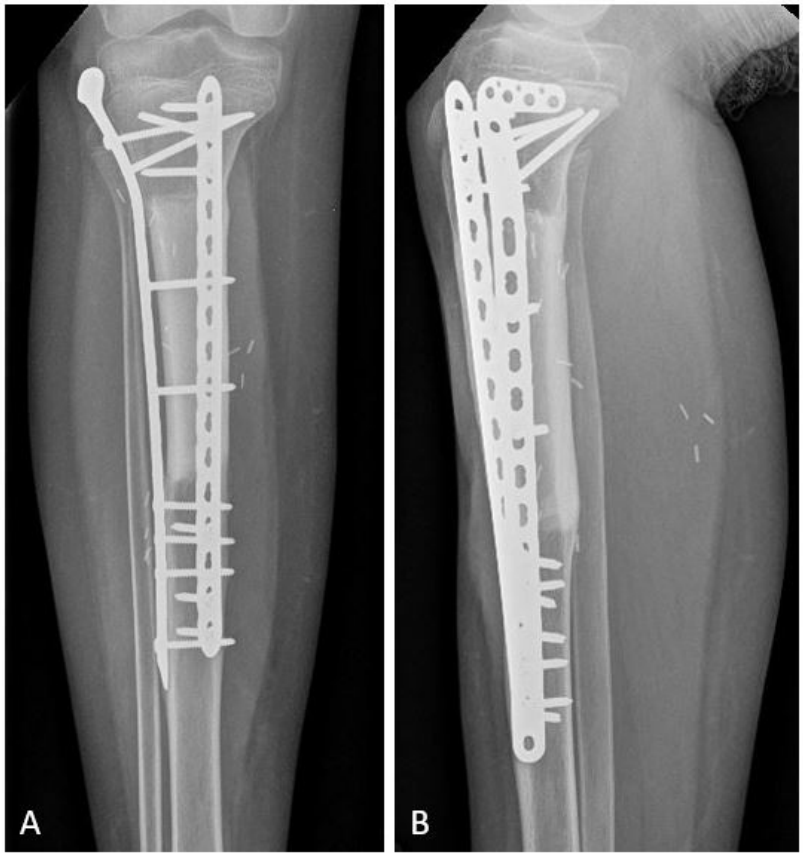


Figure 2a and 2b: Anteroposterior (a) and Lateral (b) radiographic views of the intercalary allograft 12 months postoperatively. The epiphyseal screws were removed at 3 months in order to lessen the risk of a growth disturbance. The patient was ambulating without a gait aid or pain.

PAPER 10

Revitalization and accelerated structural allograft union in femoral intercalary reconstructions with a vascularized periosteal flap. A preclinical study.

Authors: Irene Gallardo-Calero; Andrea Sallent; Matias De Albert; Alba López-Fernandez;; Sergi Barrera-Ochoa; Roberto Vélez

Institutions: Department of Orthopaedic Surgery, Hospital Vall d´Hebron, Barcelona, Spain; Department of Radiology, Hospital Vall d´Hebron, Barcelona, Spain; Musculoskeletal Engineering Research Group, Vall d´Hebron Insitut de Recerca VHIR, Barcelona, Spain; Department of Orthopaedic Surgery, Hospital Sant Joan de Deu, Barcelona, Spain

Background: With advances in early diagnosis, chemotherapy, and accurate preoperative imaging, many tumors involving the metadiaphyseal region of long bones can be treated with epiphyseal preservation. Segmental biologic reconstruction after wide resection remains a challenge in orthopaedic oncology and technical options include vascularized fibular grafts, autogenous extracorporeally irradiated bone, distraction osteogenesis, and massive allografts. Massive bone allografts, despite its common use, are not exempt from biological and biomechanical complications. Although reported clinical series show that vascularized fibular or periosteal flaps seems to be helpful in massive bone defect reconstruction there are no comparative studies or histological evidence on the effect of an additional vascularized grafts on a devitalized structural bone graft.

Questions/Purposes: In the present study, the role of a vascularized periosteal flap associated with structural bone allograft has been analyzed within a critical size defect in rat femur.

Material and Methods: Sixty-four rats were allocated to two equal groups. Within the control group, critical size defects were performed on their femurs and reconstructed with cryopreserved structural bone allograft. In the experimental group, a vascularized periosteal flap from medial femoral condyle was associated with the allograft. After 4, 6 and 10 weeks, animals were euthanized and the femurs were harvested for analysis using histology (light and confocal microscopy and backscattered electron imaging), micro CT and biomechanical evaluation, analysing the osteogenic and revitalizing properties of vascularised periosteal flap.

Results: After 10 weeks in the control group 12,5% (2/16) of the proximal osteotomies and 6.25 (1/16) of the distal osteotomies had healed compared to a significant increase in the experimental group where 56.3% (9/16) and 68.8 (11/16) in the proximal and distal osteotomies healed respectively. In contrast to the control group, where none of the samples showed new bone formation at the different time groups, there was extensive bone neoformation in the allograft surface observed in the experimental group ranging between 75-87.5% of the samples (Figure 1). In the biomechanical testing, despite not achieving equal results to the non-operated contralateral femur (maximum torque N-mm range 406.7-670.8), experimental group femurs showed a resistance pattern similar to them (maximum torque N-mm range 120.4-654.0), suggesting the allograft was osteointegrated and adopting similar features to host bone. The confocal microscopy analysis showed a lineal and structured bone apposition related to periosteal flap, synchronic with a perivascular bone apposition. Finally, both scanning electron microscopy and histology showed an intramembranous ossification produced by the vascularized periosteal graft, also showing obvious signs of revitalization of the initial allograft in the experimental group (Figure 2).

Conclusions: The vascularized periosteal graft technique promotes and accelerates osteointegration and revitalization of a structural bone allograft through intramembranous ossification, achieving histological and biomechanical features similar to host bone in a preclinical rat model. Therefore it should be considered as a complementary technique in structural bone allograft reconstructions in order to decrease the biomechanical complication rates in the clinical practice.

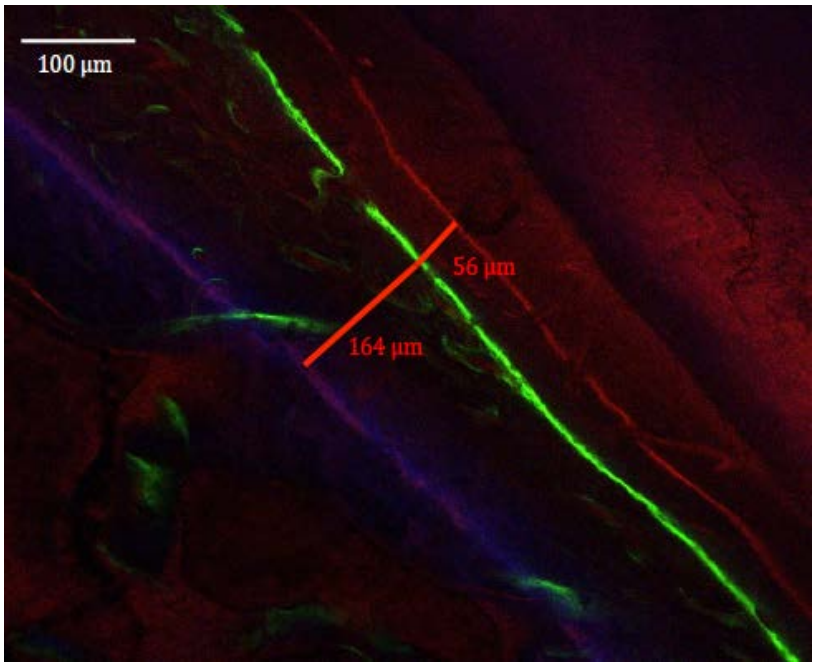
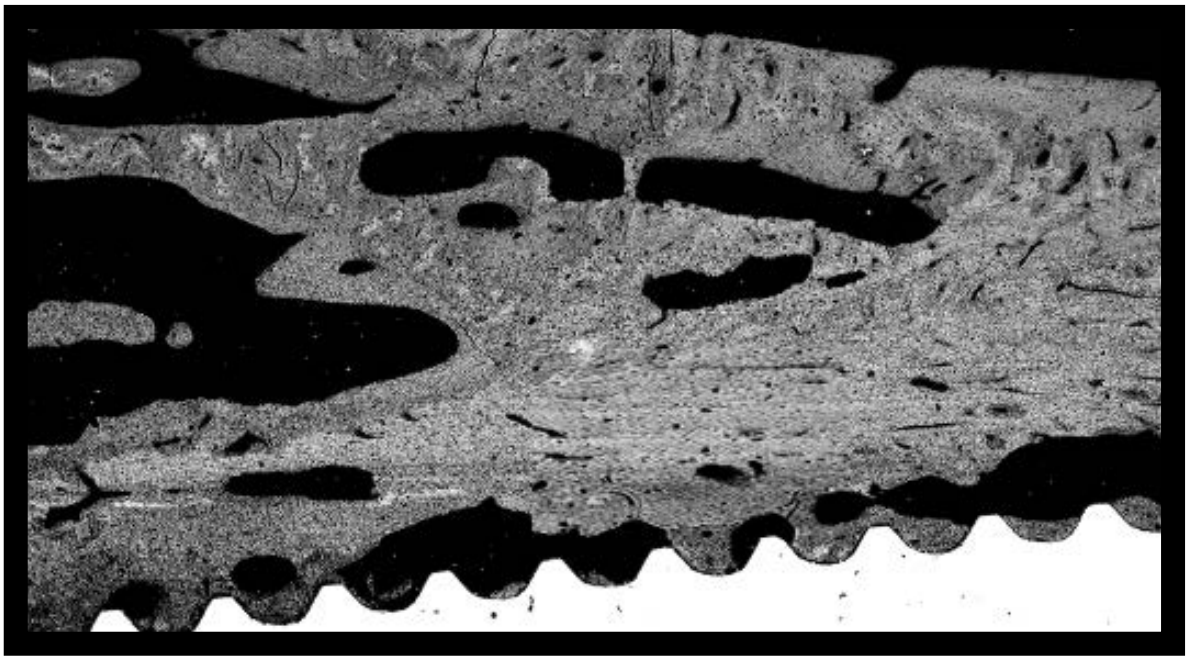


Figure 1: Linear bone neoformation in the experimental group.

Figure 2. Scanning electron microscope image of a distal femoral osteotomy sample from the experimental group at 10 weeks showing complete healing. The allograft has remodeled completely being indistinguishable from the host bone. Revitalization is evident from mineral bone aposition over the implant surging from the allograft endomedullary canal.



PAPER 11

The Long-Term Survival of Mega-Endoprosthetic Reconstructions after Two-stage Revision Surgery for Periprosthetic Joint Infection

Authors: David Hennessy MD, Joseph Schwab MD MS, Francis Hornicek MD PhD, Santiago Lozano Calderon MD PhD, Kevin Raskin MD

Institution: Massachusetts General Hospital Department of Orthopaedic Surgery

Background: Mega-endoprosthetic reconstructive surgery offers both oncologic and non-oncologic patients an important treatment option for limb salvage. Periprosthetic joint infections (PJI) are a devastating complication that affect between 2-10% of patients and commonly result in additional invasive procedures, amputation, and sometimes death. The difficulty in dealing with these infections is attributed to the elusive nature of its diagnosis and complexity of treatment. Despite this risk, mega-endoprosthetics remain a preferred treatment option. However, there is little published data evaluating the survival of mega-endoprosthetic reconstructions after two-stage revision surgery with cement spacers for the treatment of periprosthetic joint infections.

Purpose/Questions:
1. What is the survival of mega-endoprosthetic reconstructions after re-implantation following two-stage revision surgery with a cement spacer for the treatment of a PJI?
2. How does the length of the bony defect (i.e. the size of the cement spacer) affect survival of the reconstruction or future complications?
3. What is the functional status of patients following re-implantation of mega-endoprosthetics as evaluated by validated questionnaires?

Patients and Methods: This study evaluates mega-endoprosthetic reconstruction survival after PJI and two-staged reconstruction using a cement spacer. We retrospectively reviewed the charts of 22 patients (23 limbs) treated for mega-endoprosthesis infection with cement spacer between 1990 and 2017 by a group of orthopedic surgeons at a single institution. We analyzed the effect of spacer length on the survival of the prosthesis and number of associated complications. Complications included recurrent periprosthetic joint infection, prosthesis failure due to loosening or separation, and amputation. For the evaluation of functional outcomes we used patient-reported quality of life surveys EQ-5D and Lower Extre*mity Functional Scale Questionnaire.*

Results:
1. After the two-stage revision and re-implantation there was a 43% chance of complication, including eight patients treated for recurrent PJI and two patients treated for mechanical failure of the reconstruction. In this series there was a 17% chance of amputation following two-stage revision surgery.
2. Spacers of greater than 10 cm yielded 90% (9/10) of the complicated surgeries and 38% (5/13) of the non-complicated surgeries. Spacers of less than 10 cm yielded 10% (1/10) of the complicated surgeries and 62% (8/13) of the non-complicated surgeries.
3. The average LEFS was 35.5 out of 80. For the EQ-5D mobility averaged 1.9, looking after myself averaged 1.6, activities of daily life averaged 1.6, pain or discomfort averaged 1.9, and feeling worried/sad/unhappy averaged 1.5.

Conclusions: In our series 83% of patients in the study retained their limb at a minimum of two years post-operative follow up.

The data confirmed that as the size of the bony defect increases, which directly correlates to the size of the cement spacer, the patient had a higher probability of undergoing more surgeries in the future. Additionally, those limbs with complications were more likely to eventually result in an amputation. The validated questionnaires suggested moderate functionality despite the severity and invasiveness of limb salvage surgery. This information leads us to believe that a mega-endoprosthetic PJI can be successfully managed using a two-stage revision with cement spacer though the complication rate remains high and the surgeon must be mindful of how much bone is resected before re-implantation.

PAPER 12

One Stage Revision With Placement Of Local Antibiotic Carrier In The Treatment Of Modular Oncologic Joint Reconstruction

Authors: Herrick J. Siegel, MD, Jeffrey Pearson, MD, Yvonne E Chodaba, BA

Institution: University of Alabama at Birmingham Medical Center, Division of Orthopaedic Surgery

Background: Infected megaprosthesis reconstructions remains a very challenging problem. While the gold standard in total joint arthroplasty is a 2-stage revision, this may not be practical for those patients with extensive bone loss and no joint stability. The concept of a 1 stage reconstruction is gaining popularity and with current bioabsorbable antibiotic delivery systems, this may be a viable option with significantly less morbidity. The long term outcome of 1 stage revisions for infected megaprosthesis has not been well reported.

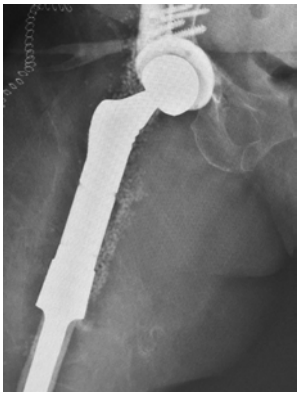
Questions/Purposes: What is the long-term success of a 1 stage revision with local antibiotic carrier and is it comparable to a 2-stage revision in patients with infected megaprosthesis? Is the morbidity less for a 1 stage vs 2 stage reconstruction? Were there fewer complications associated with 1 stage vs 2 stage revision treatment? What is the surgical technique for a 1 stage revision with local antibiotics?

Patients and Methods: Data was collected prospectively for 31 patients treated for infected megaprosthesis hip or knee joints between March 2006- May 2016. Patients with a minimum follow of 1 year were included and the average follow up was 6.2 years. Seventeen (5 hips, 11 knees, 1 total femur) were treated with one stage revision with a local antibiotic carrier (Stimulan, Biocomposites) containing vancomycin 1-2 g and Tobramycin 1.2-2.4 g (Figure 1), whereas the other 14 (3 hips, 11 knees) were treated with a 2-stage revision procedure. Infections were diagnosed based on culture and inflammatory serum markers. Patients were not randomized. Those patients with organisms that were sensitive to Vancomycin or Tobramycin were treated with one stage and those patients with insensitive organisms, 2 stage. Patients infections were defined as being adequately treated if inflammatory markers remained normal for a minimum of 6 months off antibiotics. The MSTS outcome's measure was used in all patients. All statistical analysis was performed using SAS 9.4 (SAS Institute, Inc,) and level of significance was set at 0.05. (2-sided).

Results: Two of 17 patients treated with 1 stage revision were noted to have a recurrence of infection. A relapse of MRSA infection was seen in both patients with recurrent infection. One patient at 18 months' post treatment and the other at 21 months. In the 2-stage group, 4 of 14 patients had recurrence of their infection. They were noted to have recurrent infection at 4, 11,

15, and 52 months' post op. Of these 4, 2 were treated with an above knee amputation, one with washout and antibiotic suppression, and the forth a repeat stage one revision. MSTS scores for one stage treated patients were significantly higher than those in the 2-stage group at 6 months, 12 months and 2 years post op. Patients with one stage revisions also had shorter hospitalizations and less associated complications including DVT, pneumonia and UTIs; however, the numbers were too low to determine statistical significance.

Figure 1. Post op image of stage 1 revision proximal femur replacement & acetabular reconstruction with antibiotic impregnated beads. Beads are seen along the medial aspect of the implant and in the adjacentt o the femoral head.



Conclusions: A 2 stage revision remains the gold standard for treated infected arthroplasties; however, in select patients with an infected megaprosthesis, a one stage revision with debridement and placement of local antibiotic carrier may have significant benefits. A 2-stage revision in this population can be highly morbid and is often associated with perioperative complications and prolonged hospitalizations. The 1 stage revision appears to be a viable option with potentially predictable long term success. More long term studies will be needed to determine if late relapses are significantly different between the two treatment options.

PAPER 13

Treatment Of Chronic Prosthetic Joint Infection And Concomitant Lengthening In Revision Distal Femur Replacement After Large Tumor Resection: A Case Report

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Institution: Memorial Sloan Kettering Cancer Center

Introduction: Periprosthetic joint infections (PJI) is a concerning complication in cancer patients with endoprosthesis. Not only do infections lead to increased pain and worse functional outcomes, they also necessitate repeated surgeries and lead to loss of bone stock and length, which can make future revisions less successful. Previous studies have described limb lengthening simultaneously with the surgical treatment of infections, showing lower rates of reinfection and better functional outcomes. In the United States, PJI are widely treated with two-stage revision surgery. To our knowledge, concomitant treatment of PJI and limb lengthening in a two-stage revision arthroplasty have never been describe.

Questions/Purpose: We describe a case where limb lengthening was performed during the initial sterilization stage of the two-stage revision surgery.

Patients and Methods: A 19-year old male with osteogenic sarcoma, who underwent resection and reconstruction, which was initially complicated by PJI, requiring revision and suppression of infection to allow for chemotherapy. Eight months after the completion of chemotherapy, the patient developed recurrent PJI, treated with two-stage revision arthroplasty. During the first stage of the revision, an internal lengthening intramedullary rod was placed in distal femur, allowing for simultaneous treatment of the PJI and limb lengthening.

Results: A total of 130 mm of bone was regenerated in the proximal femur, during the sterilization phase of the revision arthroplasty. Finally, the patient had a limb length discrepancy of 50 mm, which was corrected with shoe-lift. Six months after revision, the patient had no pain, an Eastern Cooperative Oncology Group (ECOG) score of 1, Musculoskeletal Tumor Society (MSTS) lower extremity score of 28, and flexion of 100 degrees. Additionally, the patient was able to ambulate independently and return to work. The regenerated bone matured without any infections or other complications. However, the patient ultimately died due to late metastatic disease to the lung.

Discussion: Our case is novel because a total of 130 mm of bone were successfully regenerated in the proximal femur during a prolonged first stage of a two-stage revision while concomitantly treating the adjacent PJI. Along with treating the infection, we restored proximal bone stock and minimized size of the implant, while allowing future correction of the limb length discrepancy.

The lengthening was performed without delaying or altering the treatment of the infection, minimizing morbidity. Additionally, our patient had good clinical outcomes with a minimal limb length discrepancy, no pain, and good functional outcomes including ECOG and MSTS.

Conclusion: This case report suggests that the problem of infection and tumor related bone loss could be addressed while treating the PJI. This leads to not only more robust bone for future surgical revisions, but also a shorter length prosthetic. The goal is to ultimately allow for better functional outcomes and lower rates of recurrent infection with endoprosthetic use.

PAPER 14

A collaborative research initiative for the establishment of the INTernational Endoprosthesis REgistry for Sarcoma Treatment (INTEREST) Study Group.

Authors

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Background: In contrast to the continuous improvement in survival rates of standard joint replacement reconstructions, endoprosthetic reconstructions continue to present poor long-term results. Although failure modes have been identified and classified, there is a general lack of knowledge of risk factors for endoprosthetic failure. Currently there are no multicenter collaborative endoprosthetic registries that could help better understand biologic and mechanical risk factors that lead to failure patterns. In a recent MSTS consensus initiative, the research question "What are the outcomes over time for orthopaedic oncology implants? (Methodology: Prospective Registry)" was the second highest voted priority in our field. Therefore we have set out to develop the INTernational Endoprosthesis REgistry for Sarcoma Treatment (INTEREST) Study Group. The main objectives of this study group are to improve reconstruction and patient function, and reduce perioperative and long-term complications.

Questions/Purposes: We surveyed international collaborators in our field in order to determine both the level of potential investigator engagement in the INTEREST Study Group and industry funding capabilities.

Methods: An online survey was created and sent to 98 research collaborators from the PARITY Study, which included questions on demographics, contact information, experience level, research support and preferred implant companies. Implant company distribution was calculated by dividing the total number of endoprostheses implanted per surgeon per year evenly between the companies they preferred. The survey was closed on March 1st 2017. Annual implant spending was estimated with average costs of a standard 15 cm distal femoral reconstruction. A descriptive analysis was performed.

Results: Fifty surgeons (52% response rate) completed the survey with an average age of 46 years (range: 35-67) and an average of 13.7 years experience in orthopaedic oncology (range: 2-34). Twenty-seven participants work in North America, 4 in South America, 13 in Europe, 1 in Africa and 5 in Asia Pacific. Participants perform 47 endoprostheses per year on average (range: 4-400) for a total of 2362 implants per year. Twenty-six percent of implants were Stanmore (n = 608), 22% ZimmerBiomet (n = 508) and 19% Stryker (n = 450). Forty-five percent of the implants were either

Stanmore or Stryker and 36 surgeons (72%) used either or both. Annual implant spending by all 50 surgeons was estimated to be approximately 20 million euros.

Conclusions: There is a solid community of international research collaborators willing to participate in the INTEREST Study Group. Annual endoprosthetic procedures within the study group could enable big data analysis from a prospective database. Considering endoprosthetic annual costs, the industry should be sought to support this project. The European Spine Study Group, founded in 2010 by an international group of collaborators with similar objectives to the INTEREST Study Group and financed through industry support, has had a progressive yearly research output with 23 indexed publications in the last 4 years. All MSTS members are invited to participate in the INTEREST Study Group and provide insight into funding opportunities.

Level of Evidence IV

PAPER 15

Is Malnutrition Associated with Postoperative Complications in Patients with Primary Bone Sarcomas?

Authors: Park A[1], Lans J[1], Raskin KA[1], Hornicek FJ[2], Schwab JH[1], Lozano Calderon SA[1]

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Background: Postoperative wound complications remain some of the most challenging problems following limb salvage surgery for bone sarcomas and may be due in part to neutropenia from chemotherapy, impaired wound healing due to radiation therapy, and poor nutritional status. Whether modifiable risk factors can be optimized to decrease postoperative complications following surgeries for bone sarcomas is unknown.

Questions/Purposes: The purpose of this study is to evaluate whether malnutrition is associated with a higher rate of postoperative complications in patients with primary bone sarcomas requiring surgical therapy.

Patients and Methods: We retrospectively identified 275 patients aged 18 and older who underwent surgery for primary bone sarcomas between 1992 and 2014. We included patients who had serum albumin values recorded within 4 weeks prior to surgery. A postoperative complication was defined as an infection, hematoma, need for additional surgery, or wound complication. Preoperative serum albumin level, total lymphocyte count (TLC), patient characteristics, tumor characteristics, and treatments were recorded. We performed a bivariate analysis to evaluate if the aforementioned factors were associated with postoperative complications. For variables with $P < 0.1$, we performed logistic regression for multivariate analysis with $P < 0.05$ considered to be statistically significant.

Results: Of the 275 patients, there were 173 patients with osteosarcoma, 66 with chondrosarcoma, 15 with Ewing's sarcoma, and 21 with other types of sarcomas. In the bivariate analysis, age, TLC < 1000 cells/mm^3, albumin < 2.7 g/dL, neoadjuvant chemotherapy, neoadjuvant radiotherapy, and location in the pelvis were associated with postoperative complications ($P < 0.05$). In the multivariate analysis, age ($P = 0.04$), pelvic location ($P = 0.04$), and neoadjuvant radiotherapy ($P = 0.008$) were independently associated with postoperative complications. We then performed a sub-analysis of patients without a pelvic tumor or history of

neoadjuvant radiotherapy (n = 178). In this population, albumin < 2.7 g/dL was found to be independently associated with postoperative complications (odds ratio = 4.69, 95% confidence interval = [1.03-21.34], P = 0.04).

Conclusions: This study demonstrates that hypoalbuminemia (albumin < 2.7 g/dL) is independently associated with postoperative complications in patients with extremity bone sarcomas who do not receive neoadjuvant radiotherapy. Future studies are necessary to further elucidate the role of nutrition, and they may show that nutritional status is a modifiable risk factor that can be optimized to improve the outcome of surgery for primary bone sarcomas.

Table 1

Table 1: Bivariate Analysis Postoperative Complications All Patients			
		All Complications	
Variable	Yes (n=70)	No (n=205)	
Age, median (IQR)	29 (16-53)	39 (23-54)	
p-value[1]			***0.0099***
Diagnosis			
Osteosarcoma	47 (27.2)	126 (72.8)	
Chondrosarcoma	13 (19.7)	53 (80.3)	
Soft tissue sarcoma	4 (36.4)	7 (63.6)	
Ewing's sarcoma	4 (26.7)	11 (73.3)	
MFH	2 (22.2)	7 (77.8)	
Metastasis	0	1 (100)	
*p-value**			*0.78*
Albumin <2.7	*7 (50.0)*	7 (50.0)	
*p-value**			***0.030***
TLC<1000	31 (33.7)	61 (66.3)	
*p-value**			***0.026***
Treatment related factors			
Location			
Femur	20 (19.6)	82 (80.4)	
Pelvis	25 (41.0)	36 (59.0)	
Tibia	9 (25.0)	27 (75.0)	
Vertebra	7 (33.3)	15 (66.7)	
Humerus	5 (29.4)	12 (70.6)	
Scapula	1 (10.0)	9 (90.0)	
Below the knee	2 (14.3)	12 (85.7)	
Other	1 (7.1)	13 (92.9)	
*p-value**			***0.035***
Neoadjuvant chemotherapy	49 (31.0)	21 (18.0)	
*p-value**			***0.014***
Neoadjuvant radiotherapy	22 (50.0)	48 (20.8)	
*p-value**			***<0.001***

* Using Chi-squared test

Table 2

Table 2: Subanalysis: Logistic Regression for Postoperative Complications in Patients Without Radiotherapy or Pelvic Tumor				
Variable	**Odds Ratio**	**Standard error**	**95% Confidence Interval**	***P*Value**
Age	0.97	0.013	[0.95, 1.0]	0.058
TLC <1000	1.50	0.64	[0.65, 3.46]	0.34
Albumin <2.7	4.69	3.62	[1.03, 21.34]	**0.045**
Neoadjuvant chemotherapy	1.54	0.83	[0.54, 4.41]	0.42
Adjuvant chemotherapy	1.46	0.78	[0.52, 4.09]	0.47

Area under the receiver operating characteristic curve = 0.73

Pseudo R2, 0.090

P-value for Hosmer-Lemeshow test, 0.21

PAPER 16

Bulk allograft is more susceptible to infection than is stainless steel or cancellous allograft using a mouse model of infection

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Introduction: Bulk allograft remains a viable reconstruction option for large bone defects, with infection being a devastating complication. Other frequently used options for filling bone defects include stainless steel implants and cancellous bone allograft chips. Currently, infection treatment principles are similar amongst all implant materials based on empiric data demonstrating similar infection rates between allograft and stainless steel.

Purpose: The purpose of this study was to use our previously established mouse model for real-time quantification of bulk allograft infection in order to assess susceptibility to infection in bulk allograft compared to cancellous allograft and stainless steel. We sought to ask: 1) is cortical allograft equally susceptible to infection as is cancellous allograft? and 2) is cortical allograft equally susceptible to infection as is stainless steel?

Methods: We implanted a 2.5mm cortical allograft, cancellous allograft chip, or stainless steel disc in a subcutaneous pocket dorsal to the cervical spine in C57BL/6 wildtype mice. The implant was inoculated with doses of either $1*10^2$ or $1*10^3$ colony forming units (CFUs) of bioluminescent Xen36 *Staphylococcus aureus* in 2ul phosphate buffered solution. *In vivo* bioluminescence imaging was performed over 56 days. Enumeration of CFUs, explantation, histologic analyses, and Live-Dead assay confocal microscopy were performed at critical time points. Statistics were performed via t-test and ANOVA analysis.

Results: Both inoculums on bulk allograft generated both an early peak (seven – ten days) and late peak (18 – 35 days) in infection. Both inoculums on stainless steel and cancellous allograft only generated a single peak that returned to sterile control levels for the duration of the experiment. Bulk allograft infection magnitude was significantly higher than stainless steel and cancellous allograft at both peaks and final infection time point ($p < 0.05$). Enumeration of CFUs and live-dead assays corroborated the bioluminescent findings. Explantation and histologic analyses of cortical allograft demonstrated a hypervascular capsular response in the infected bulk

allograft implants at POD18 and POD35, as well as bacterial invasion of cortical bone architecture at POD56 that was not present earlier. Sterile cortical specimens lacked an inflammatory capsule or bacterial invasion on histology.

Discussion and Conclusion: Unexpectedly, bulk allograft implants demonstrated significantly higher susceptibility to infection than either stainless steel or cancellous allograft in this mouse model of subcutaneous implant infection. Infected bulk allograft specimens demonstrated a hypervascular, inflammatory capsule that was not present in sterile specimens. Ramifications of the mouse model include the ability to modulate host variables through genetic manipulation, allowing further elucidation of infection mechanism.

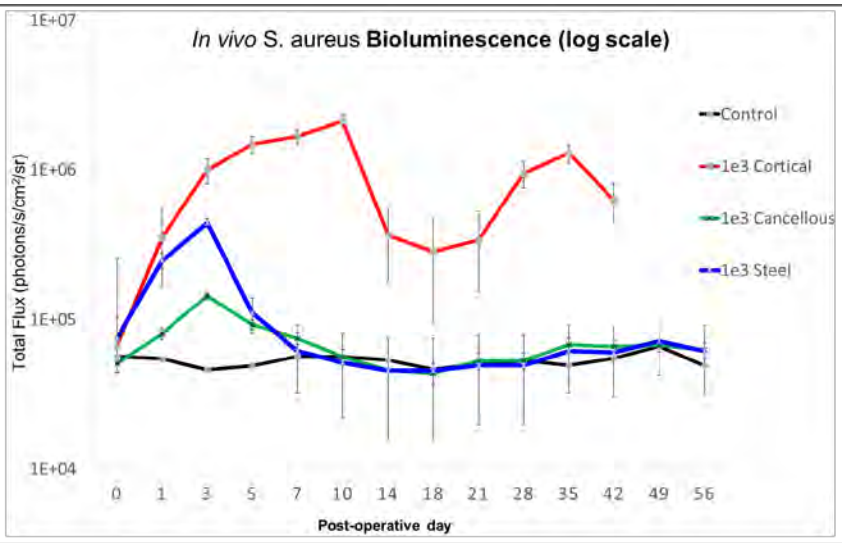

Figure 1. Measurement of bacterial burden using in vivo bioluminescence. *S. aureus* possessing the bioluminescent construct in a stable plasmid (Xen36) in one inoculum ($1*10^3$ CFU) or no bacteria as a control were inoculated into the dorsal cervical subcutaneous space of mice in the presence of either a cortical allograft implant, cancellous allograft implant, or stainless steel disc. Bacterial counts as measured by in vivo *S. aureus* bioluminescence (mean maximum flux [photons/s/cm2/sr]sem [logarithmic scale]). Cortical experiment ended at POD42 due to severe wound breakdown.

Figure 2. Cortical Allograft Histology

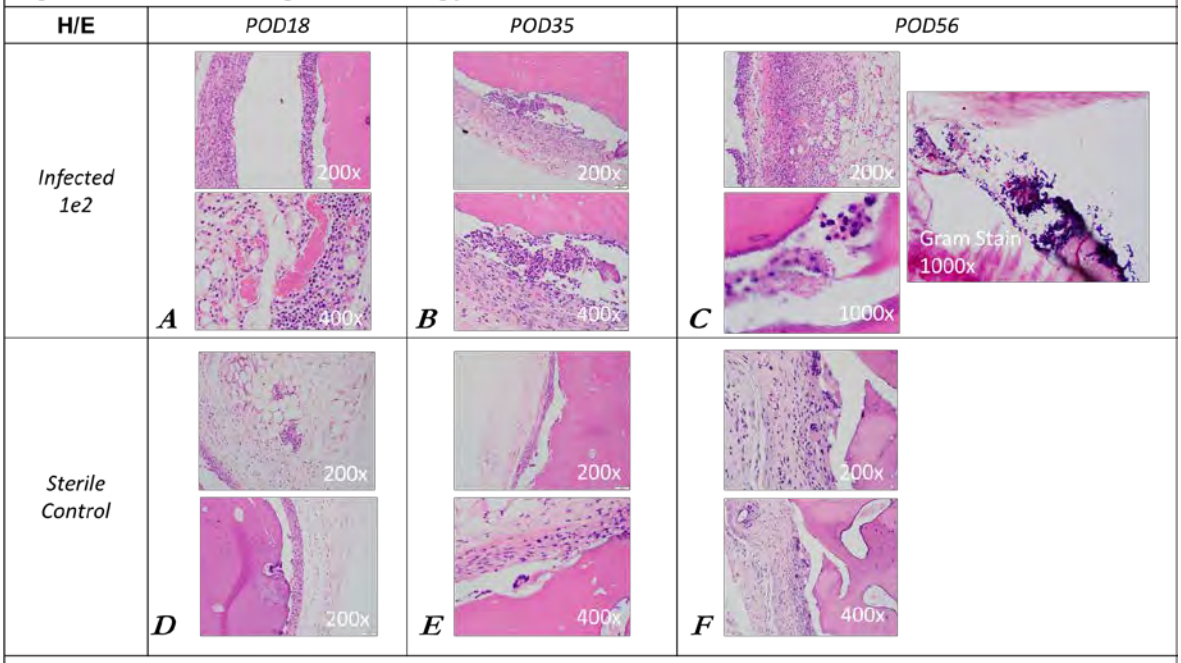

Figure 2. Cortical allograft histology. (A)-(C): Inoculated with $1*10^2$ CFU *S. aureus*. (D)-(F): Sterile control. (A): POD18, 200x and 400x, thick inflammatory capsule and evidence of neovascularization in cortical bone; (B): POD35, 200x and 400x, thick inflammatory capsule and evidence of neovascularization in cortical bone; (C): POD56, 200x, neovascular formation within thick capsule and extensive inflammatory reaction, 1000x, bacterial cocci within haversian canal, and 1000x, gram stain demonstrating gram positive cocci within haversian canal; (D): sterile POD18, 200x and 400x, thin inflammatory capsule, no evidence of bacteria (E): sterile POD35, 200 and 400x, thin inflammatory capsule, no evidence of bacteria, and a multinucleated giant cell with resorption pit; (F): sterile POD56, 200x and 400x, thin inflammatory capsule, no evidence of bacteria.

PAPER 17

Soft Tissue Sarcoma and Time to Treatment: An Analysis of the National Cancer Database

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Background: The time to treatment interval (TTI), defined as the period from diagnosis to first definitive treatment, has very limited descriptions toward understanding delays in soft tissue sarcoma (STS) care. As TTI becomes an important quality control metric across institutions, a better understanding for delays in STS treatment initiation is crucial.

Questions/Purposes: 1) What is the current national standard for time to definitive treatment in STS diagnoses? 2) What characteristics are associated with TTI variability in patients with STS?

Patients and Methods: The National Cancer Database (NCDB) was utilized for this retrospective study. A total of 46,274 patients with primary STS diagnosed between 2004 and 2013 were identified using International Classification of Disease for Oncology, Third Edition [ICD-O-3] topographical and histological codes. Pediatric patients (<18 years old) were not available from this database. Patients were excluded if they did not receive definitive treatment (n = 4,695) in the form of surgery, systemic therapy, radiotherapy, or other type of definitive treatment (i.e., clinical trial enrollment). Non-curative surgical treatments were not considered definitive therapy. Patients with a TTI > 365 days (n =47) were also excluded as outliers. The final analysis included 41,529 patients. Univariate analysis was conducted using Kruskall-Wallis tests to identify differences within the variables regarding TTI. A negative binomial regression model was used to identify what patient, tumor, and treatment variables are independent risk factors for delaying TTI.

Results: The median time to treat was 22 days. The median age was 60 years old (range 18-90). Approximately 57% of patients were definitively treated in the same center where the index diagnosis was made. The most common diagnoses were undifferentiated pleomorphic sarcoma/malignant fibrous histiocytoma (26%), liposarcoma (16%) and spindle cell sarcoma (7%). Grade 1 histology (9%) was less common than higher grade (2, 3; 64%) histology, and the most common primary tumor sites were the lower extremity/hip (40%) and trunk (32%). The most common initiating treatment modality was surgery (68%), followed by radiotherapy (16%) and systemic therapy (15%).

In univariate analysis, patient factors that led to differences in TTI included age ($P<0.001$) and distance from facility ($P<0.001$). Healthcare variables that led to differences in TTI included insurance type ($P<0.001$), facility type ($P<0.001$), transition in care ($P<0.001$), year of diagnosis

(P<0.001), and first-line treatment modality (P<0.001). Tumor characteristics that led to differences in TTI include histology (P<0.001), primary site (P<0.001), size (P<0.001), grade (P<0.001), and stage (P=0.033).

Following multivariate-analysis, TTI was found to be influenced by several factors. Longer TTI was correlated with the following patient, tumor and treatment factors, by descending influence: having a transition in care (Incidence rate ratio [IRR]=1.76; P<0.001), receiving radiotherapy (IRR=1.42; P<0.001) or systemic therapy (IRR=1.24; P<0.001) first, seeking care at an academic center (IRR=1.22; P<0.001), Medicaid insurer (IRR=1.20; P<0.001), being uninsured (IRR=1.15; P<0.001), Medicare insurer (IRR=1.07; P<0.001), a diagnosis of spindle cell sarcoma (IR=1.08; P=0.006), a primary tumor site of the upper extremity (IRR=1.06; P=0.010), non-white race (IR= 1.06; P=0.003), a primary tumor site of the lower extremity (IRR=1.05; P=0.002), and female gender (IRR=1.03; P=0.031). Shorter TTI was correlated with the following patient, tumor and treatment factors, by descending influence: having surgery (IR=0.68; P<0.001) as the index treatment, receiving treatment at a comprehensive cancer center (IR=0.87; P<0.001), tumor size >8 cm (IR=0.91; P<0.001), age >30 years (IR=0.92; P=0.002), private insurer (IR=0.92; P<0.001), a diagnosis of liposarcoma (IR=0.94; P=0.028), higher tumor grade (IR=0.94; P<0.001), a primary tumor site of the trunk (IR=0.96; P=0.004), and median income >$48,000 (IR=0.97; P=0.020).

Conclusions: The national median for TTI of STS is 22 days. Delays in TTI in STS are associated with socio-economic, healthcare, and tumor characteristics. Transitions in care between institutions are responsible for the greatest delays in STS TTI. As TTI is more commonly used as a quality metric, physicians need to be aware of the causes as we work to improve national delays in diagnosis and treatment initiation.

Table 1. Time to Treatment Initiation and Patient Demographics

	Number of Patients (%)	Median TTI, days (IQR)	P-Value
Total Number of Patients	41529	22 (0 - 42)	
Age, years			0.001
Median, [range]	60 [18-90]		
18-30	3632 (9)	21 (1, 42)	
31-50	9577 (23)	22 (0, 41)	
51-70	15583 (38)	23 (2, 42)	
71+	12737 (31)	23 (0, 43)	
Sex			0.645
Male	23183 (56)	22 (0, 42)	
Female	18346 (44)	22 (0, 42)	
Race			0.444
White	34935 (84)	22 (0, 42)	
Black	4463 (11)	23 (0, 44)	
Other/Unknown	2131 (5)	22 (0, 43)	
Charlson/Deyo Score			0.611
0	34258 (83)	22 (0, 42)	
1	5780 (14)	23 (0, 43)	
≥ 2	1491 (4)	21 (0, 42)	
Histology			<0.001
Spindle Cell Sarcoma	2888 (7)	26 (7, 48)	
Undifferentiated Pleomorphic Sarcoma (MFH)	10589 (26)	23 (3, 40)	
Liposarcoma	6507 (16)	21 (0, 40)	
Other	21545 (52)	22 (0, 43)	
Facility Type			<0.001
Community Cancer Program	2495 (6)	16 (0, 36)	
Comprehensive Community Cancer Program	11644 (28)	18 (0, 36)	
Academic Center	18132 (44)	28 (10, 47)	
Integrated Network Cancer Program	2210 (5)	21 (0, 39)	
Other/Unknown	7048 (17)	21 (0, 42)	
Insurance			<0.001
Uninsured	1759 (4)	22 (0, 45)	
Private Insurance	19147 (46)	22 (0, 40)	
Medicaid	2737 (7)	24 (2, 48)	
Medicare	16044 (39)	23 (0, 42)	
Other/Unknown	1842 (4)	29 (9, 50)	
Income			0.001
< $38,000	6889 (17)	22 (0, 43)	
$38,000 - $47,999	9460 (23)	23 (0, 43)	
$48,000 - $62,999	10888 (26)	23 (0, 42)	

$63,000+	13542 (33)	22 (0, 40)	
Unknown	750 (2)	21 (0, 42)	
Distance from Facility			<0.001
< 21 miles	24555 (59)	21 (0, 40)	
21-50 miles	7380 (18)	25 (5, 43)	
51-100 miles	4055 (10)	26 (8, 46)	
>100 miles	4302 (10)	28 (11, 48)	
Unknown	1237 (3)	23 (0, 43)	
Transition in Care			<0.001
Yes	18042 (43)	33 (17, 53)	
No	23487 (57)	14 (0, 32)	
Year of Diagnosis			<0.001
2004	3591 (9)	20 (0, 39)	
2005	3760 (9)	20 (0, 40)	
2006	3768 (9)	21 (0, 40)	
2007	3991 (10)	22 (0, 42)	
2008	4078 (10)	22 (0, 42)	
2009	4235 (10)	22 (0, 42)	
2010	4396 (11)	23 (0, 43)	
2011	4360 (11)	24 (1, 42)	
2012	4637 (11)	25 (3, 44)	
2013	4713 (11)	26 (5, 44)	
Primary Tumor Site			<0.001
Head/Neck	3467 (8)	23 (0, 46)	
Upper Extremity/Shoulder	6038 (15)	25 (0, 45)	
Lower Extremity/Hip	16540 (40)	24 (8, 42)	
Trunk	13383 (32)	21 (0, 42)	
Other	2101 (5)	14 (0, 36)	
Tumor Size			<0.001
≤ 5.0 cm	11741 (28)	22 (0, 44)	
> 5.0 cm	29788 (72)	22 (3, 41)	
Grade			<0.001
1, Well Differentiated	3525 (9)	20 (0, 43)	
2, Moderately Differentiated	4701 (11)	24 (0, 44)	
3, Poorly Differentiated	12574 (30)	22 (3, 41)	
4, Undifferentiated	9468 (23)	23 (7, 42)	
Unknown	11261 (27)	22 (0, 43)	
Clinical Staging			0.033
Stage I	1859 (5)	22 (0, 43)	
Stage II	1373 (3)	23 (0, 42)	
Stage III	8082 (20)	25 (12, 42)	
Stage IV	4601 (11)	24 (9, 42)	
Unknown	25614 (62)	22 (0, 43)	
First-Line Treatment Modality			<0.001
Surgery	28307 (68)	16 (0, 39)	
Radiation	6556 (16)	32 (21, 48)	
Systemic	6068 (15)	28 (17, 44)	
Other	55 (0.1)	24 (9, 37)	
Multi-modal	543 (1)	31 (17, 48)	

Table 2. Multivariable Model

	Incidence Rate Ratio on TTI (95% CI)	P-Value
Age (>30 years)	0.92 (0.87, 0.97)	0.002
Sex (Female)	1.03 (1.00, 1.06)	0.031
Minority Race	1.06 (1.02, 1.11)	0.003
Deyo Score ≥ 1	1.03 (0.99, 1.07)	0.141
Histology		
Spindle Cell vs all other diagnoses	1.08 (1.02, 1.14)	0.006
UPS (MFH) vs all other diagnoses	0.98 (0.93, 1.03)	0.505
Liposarcoma vs all other diagnoses	0.94 (0.89, 0.99)	0.028
Facility Type		
Academic Center vs any other institution	1.22 (1.19, 1.26)	<0.001
Comprehensive Cancer Center vs others	0.87 (0.84, 0.90)	<0.001
Insurance		
Uninsured vs Private Insurance	1.15 (1.07, 1.23)	<0.001
Private Insurance vs all others	0.92 (0.90, 0.95)	<0.001
Medicaid vs Private Insurance	1.20 (1.13, 1.28)	<0.001
Medicare vs Private Insurance	1.07 (1.03, 1.10)	<0.001
Income > $48,000	0.97 (0.94, 0.99)	0.020
Distance to facility ≥21 miles	0.97 (0.94, 1.01)	0.101
Transition in Care	1.76 (1.71, 1.81)	<0.001
Primary Tumor Site		
Head	1.02 (0.97, 1.07)	0.502
Upper Extremity	1.06 (1.01, 1.10)	0.010
Lower Extremity	1.05 (1.02, 1.08)	0.002
Trunk	0.96 (0.93, 0.99)	0.004
Tumor Size		
> 8.0 cm	0.91 (0.88, 0.94)	<0.001
Grade		
Overall grade	0.99 (0.98, 1.00)	0.024
Grade 3 or 4	0.94 (0.91, 0.97)	<0.001
Clinical Staging		
Stage overall	1.00 (1.00, 1.01)	0.429
Stage II or III	1.00 (0.93, 1.07)	0.905
First-Line Treatment Modality		
Surgery vs other tx	0.68 (0.66, 0.70)	<0.001
Radiation vs other tx	1.42 (1.36, 1.48)	<0.001
Systemic vs other tx	1.24 (1.19, 1.29)	<0.001

****Incidence Rate Ratio means for every 1 point increase in the independent variable, the rate of**

time to treatment initiated (in days) would change by a factor of that value while holding all of the other variables in the model constant.

PAPER 18

Vacuum-Assisted Closure in Sarcoma Resection May Improve Wound Complication Rates in Proximal Lower Extremity Tumors Treated With Preoperative Radiation

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Background: Although preoperative radiation (RT) followed by wide local excision yields excellent rates of local control in soft tissue sarcomas (STS), wound complication rates are significantly higher compared to post-operative RT. Proximal lower extremity STS, especially of the medial compartment, are also at an inherently higher risk of post-operative wound complications (WCs). Thus, surgeons may avoid preoperative RT due to high rates of WCs and potential need for further operations to manage morbidity. Vacuum (VAC)-assisted closure may improve wound healing through several mechanisms. Various factors may decrease the rate of WCs in STS, however, it is unknown if VAC-assisted closure during STS resection may impact this outcome and disease control.
Questions/Purposes: The goal of this study is to 1) evaluate whether increasing use of wound VAC application at the time of STS resection influences the rate of WCs and 2) determine if VAC-assisted closure affects local control rates.

Patients and Methods: From 2000-2016, 130 patients with stage I-III STS of the proximal lower extremity were treated with preoperative RT +/- chemotherapy followed by limb-sparing resection. Patient, demographic, and treatment variables, including VAC application, and wound outcomes were retrospectively reviewed. Patients excluded from the study were those that were <18 years old, STS of locations other that the proximal lower extremity, bone sarcomas, aggressive fibromatosis, or dermatofibrosarcoma protuberans. WCs were defined as those requiring operation, prolonged wound care, or antibiotics ≤ 4 months after surgery. Proximal lower extremity tumors were defined as those STS located in the anterior, posterior, medial or lateral thigh compartments. VAC-assisted closure took place at the time of primary resection. Predictors for WCs were evaluated using fisher exact test for univariate analysis (UVA) and logistic regression for multivariate analysis (MVA).

Results: Median follow-up was 3.9 years. Median age at diagnosis was 58 and median tumor size was 10.2 cm. Median preoperative RT dose was 50 Gy. Forty-four (34%) patients underwent neoadjuvant chemotherapy. Fifty-three (41%) patients had proximal medial thigh tumors. Forty-six (35%) patients with proximal lower extremity STS had a wound VAC placed

at the time of their primary resection, with 39 (85%) of these placed as incisional VACs and 7 placed as initial closure followed by a planned staged flap reconstruction.

Local control was 98%. The overall WC rate for proximal lower extremity and proximal medial lower extremity STS was 32% (41/130) and 28% (15/53), respectively. WC rates for proximal lower extremity STS from 2000-2005, 2006-2010, and 2011-2016 were 51% (15/31), 28% (14/50), and 26.5% (13/49), respectively. WC rates for medial compartment STS from 2000-2005, 2006-2010, and 2011-2016 were 60% (9/15), 19% (3/16), and 13.6% (3/22), respectively.

The frequency of VAC-assisted closures of proximal lower extremity tumors from 2000-2005, 2006-2010, and 2011-2016 were 6% (2/31), 36% (18/50), and 53% (26/49), respectively. The frequency of VAC-assisted closures of proximal medial lower extremity compartment STS from 2000-2005, 2006-2010, and 2011-2016 were 7% (1/15), 56% (9/16), and 68% (15/22), respectively. Variables associated with WCs are located in Table 1.

On UVA ($p<0.0001$) and MVA ($p=0.004$, OR 0.129, 95% CI 0.041-0.398) VAC-assisted closure was associated with decreased rates of post-operative WCs. The WC rate in patients with proximal lower extremity STS with VAC closure at the time of resection was 9% (4/45) versus 43.5% (37/85) in those who did not have VAC-assisted closure at the time of resection. The WC rate in patients with medial compartment STS with VAC-assisted closure at time of resection was 8% (2/24) versus 48% (14/29) in those who did not have VAC-assisted closure at the time of resection.

Conclusions: Proximal lower extremity STS treated with preoperative RT are at a high risk of post-operative WCs. This study has revealed that VAC-assisted closure at the time of resection of proximal lower extremity STS is associated with lower wound complication rates without compromising local control. Aggressive operative and post-operative wound management is warranted in any STS case, and the use of VAC-assisted closure may play a particularly important role in STS of the proximal lower extremity.

Variable	P-value
Age	NS
Performance Status	NS
Diabetes	NS
Cardiovascular Disease	NS
BMI	NS
Smoking	NS
Tumor Location	NS
Tumor Size	NS
Neoadjuvant Chemotherapy	NS
Flap Reconstruction	NS
Vacuum-Assisted Closure	p<0.0001

Table 1: Predictors for Post-operative Wound Complications
NS: Not significant

PAPER 19

Morbid Obesity Significantly Increases The Risk Of Postoperative Wound Complications Following Upper Extremity Limb Salvage Surgery

Authors: Matthew T. Houdek, Anthony M. Griffin, Peter C. Ferguson, Jay S. Wunder

Institution: Division of Orthopedic Surgery, University of Toronto, Mount Sinai Hospital

Introduction: Obesity is a known risk factor for wound complications and postoperative infection. Due to the increased risk of infection and postoperative wound complications, some institutions in North America are refusing to perform elective joint replacement surgery on obese patients, citing obesity as a modifiable risk factor. Unlike arthroplasty procedures, excision of soft-tissue sarcomas is not an elective procedure, and in this situation obesity is not a modifiable risk factor. Although multiple studies have examined the risk of obesity on wound healing and infection in multiple areas related to orthopedic surgery, there is a relatively paucity of data concerning its impact on sarcoma surgery.

Purpose: The purpose of this study is to investigate the impact of obesity on the outcome of upper extremity limb salvage surgery with a focus on (1) postoperative complications (2) oncologic outcome, (3) rates of limb salvage, and (4) patient function.

Method: 290 patients were identified from our institution with a histologically confirmed soft-tissue sarcoma of the upper extremity or hip girdle from 2006-2014. Follow-up data included clinical and oncologic outcome focusing on complications, local recurrence, and mortality after treatment. The mean follow-up of 4 years (range 3 months-10 years).

There were 181 males and 109 females, with a mean age of 56 years (18-97 years) and mean body mass index of 26.5 kg/m^2 (range 15.4-41.8 kg/m^2), with 67 (23%) patients being classified as obese (BMI $\geq$30 kg/m^2). Prior to surgery 151 (52%) underwent preoperative and 14 (5%) postoperative radiotherapy. The mean tumor size was 6 cm (range 0.6-28 cm) and mean volume was 328 cm^3 (range 0.1-14,053 cm^3). 145 (50%) tumors were deep to the fascia with 125 (43%) considered high grade with the most common location being the shoulder girdle (n=112, 39%). The margins were classified as negative (RO, n=239, 82%) or positive (R1, n=50, 17% or R2, n=1, 1%). 175 (60%) patients were closed primarily, 83 (29%) required a flap (58 rotational and 25 free) and 32 (11%) required a split-thickness skin graft. The mean operative time was 4 hours (range 1-18 hours). There was no difference in the mean operative time between obese and non-obese patients (4.2 vs. 3.9 hours, P=0.36).

Results: Following the procedure 58 (20%) patients sustained a postoperative complication, with 47 (16%) complications being with-in 30-days. The most common complication was a wound complication (delayed healing or dehiscence, n=30, 10%). Complications resulted in a reoperation in 46 (16%) patients, most commonly an irrigation and debridement of a wound complication (n=18, 6%).

The 5-year overall- and disease free survival were 79% and 74%. Disease recurrence was classified as isolated local (n=11, 4%), distant (n=45, 15%) and combined local and distant (n=5, 2%). The 5-year local and distant disease free survival were 92% and 82%.

Obesity was not associated with the development of a postoperative wound complication (HR 1.24, 95% CI 0.54-2.64, *P*=0.58) or a postoperative infection (HR 0.88, 95% CI 0.28-2.25, *P*=0.80); however when specifically examining morbidly obese (BMI≥40 kg/m^2) patients, there was a significantly increased risk of wound complications (HR 8.12, 95% CI 1.31-27.13, *P*=0.02). Likewise obesity was not associated with local recurrence (HR 0.68, 95% CI 0.15-2.14, *P*=0.53) or the ability to achieve a negative margin (OR 0.70, 95% CI 0.19-2.58, *P*=0.76). Additionally, increased operative time >5 hours (HR 3.35, 95% CI 1.59-7.51, *P*=0.001), increased the risk of a wound complication, however preoperative radiotherapy did not (HR 1.56, 95% CI 0.75-3.39, *P*=0.23). However, preoperative radiotherapy was associated with a postoperative infection (HR 2.87, 95% CI 1.12-8.78, *P*=0.02).

At last follow-up the mean TESS and MSTS93 scores were 91 (range 40-100) and 94% (range 57-100). There was no difference in the mean TESS (93 v. 90, *P*=0.28) or MSTS93 (95% v 93%, *P*=0.39) between obese and non-obese patients.

Conclusion The results of this study indicate that along with previously established risk factors for a postoperative wound complication (operative time length); morbid obesity significantly increased the risk of a postoperative wound complications. Although morbidly obese patients are at increased risk of a wound complication, they were not at an increased risk of an infection. In addition, obesity did not hinder the ability to achieve a negative margin or significantly affect functional outcome.

PAPER 20

Does the Modality of Radiation Therapy Used to Treat Liposarcomas of the Extremities Impact the Outcome?

Authors: Park A, Hill S, Baker J, Bernstein K, Lozano Calderon SA.

Institution: Massachusetts General Hospital

Introduction/Background: Radiation therapy techniques for soft tissue sarcomas have evolved. Studies demonstrated differences in wound complication rates and functional outcomes when preoperative and postoperative radiation therapy were compared. Modern techniques such as intensity modulated radiation therapy (IMRT) and 3 dimensional conformal radiation therapy (3D-CRT) minimize the dose to neighboring tissues, thereby minimizing treatment side effects when compared to conventional photon therapy. However, it remains unknown whether outcomes are improved when such techniques are used to treat liposarcomas.

Question/Purpose: The purpose of this study is to compare clinical outcomes and complication rates among IMRT, 3D-CRT and older radiation techniques like 2D-CRT in a homogenous population of patients with liposarcomas of the extremities. Secondarily, we compared outcomes for radiation therapy delivered at a tertiary referral center compared to community hospital based facilities.

Patients/Materials: After obtaining IRB approval, we performed a retrospective chart review of all the patients treated for liposarcomas of the extremities at our institution between 1990 and 2015. Patients older than 18 years of age and with histological confirmation of any type of liposarcoma of the extremities were included in the study, with the exception of well-differentiated low-grade liposarcoma. Demographic data, clinical presentation, histology, grade, size, location, timing of treatment, radiation technique, complications, and local control rates were collected.

Statistical analysis included estimation of distribution of the data. Comparisons in terms of local control and complications were performed by contrasting patients who received IMRT/3D-CRT vs. those who received 2D-CRT. Additionally, we performed the same analysis comparing patients treated at our institution with those treated at non-tertiary outside facilities.

Results: A total of 126 patients were identified. Of these, 61 (48%) were females. Median age was 49.5 years (range: 18-87). The most prevalent histology was myxoid liposarcoma (54%), and 94% of all tumors were located in the lower extremity. One hundred and eleven patients presented for initial treatment at our institution (88%). Of these, only two (1.6%) had metastatic disease at presentation. Fifteen patients (12%) were seen after intralesional resection or recurrence after an oncologic resection at an outside hospital. Seventy four patients (59%)

received preoperative radiation only, 6 (4.8%) received postoperative radiation only, and 29 (23%) received pre- and postoperative radiation. Seventy one patients (64%) received radiation at a tertiary referral center (Table 1).

We did not identify any differences in local recurrence, infection, and wound dehiscence between IMRT, 3D-CRT, and 2D-CRT ($p = 0.48$). We did find a lower infection rate in patients treated at a tertiary care facility (22%) when compared to a non-tertiary referral center (32%), but this was not statistically significant ($p = 0.27$)

Conclusion: We were unable to demonstrate any statistically significant differences in outcomes based on the modality of radiation therapy used. While the infection rate was lower in patients treated at a tertiary care facility, this finding was not statistically significant. Further investigation is warranted to further elucidate the role that treatment at a tertiary referral center may play in the outcomes of liposarcomas of the extremities treated with radiation therapy.

Table 1 (Demographics)		
Total of Patients	126	100.0%
Age (Median and Range)	49.5	R: 18 - 87
Gender	**126**	**100.0%**
Female	61	48.0%
Male	65	52.0%
Location	**126**	**100.0%**
Upper Extremity	**7**	**5.6%**
Axilla	1	0.8%
Shoulder	5	4.0%
Arm	1	0.8%
Lower Extremity	**119**	94.4%
Gluteal	12	9.5%
Thigh	81	64.3%
Knee and below	23	18.3%
Tumor Histology	**126**	**100.0%**
Dedifferentiated	13	10.3%
Myxoid	68	54.0%
Pleomorphic	14	11.1%
Round Cell	4	3.2%
Conventional	4	3.2%
Mixed*	23	18.3%
Myxoid/Round Cell	17	[74%]
Myxoid/Well Diffentiated	1	[4.5%]
Myxoid/Dedifferentiated	1	[4.5%]
Round Cell/Pleomorphic	2	[9.0%]
Myxoid/Round Cell/Pleomorphic	1	[4.5%]
Myxoid/Round Cell/Pleomorphic/Dedifferentiated	1	[4.5%]
Tumor Grade	**126**	**100.0%**
Grade I	11	8.%%
Grade I-II	12	9.5%
Grade II	67	53.2%
Grade II-III	20	15.9%

Grade III	15	11.9%
Unknown	1	0.8%
Clinical Presentation	**126**	**100.0%**
Tumor not previously treated without metastatic disease at presentation	109	86.0%
Tumor not previously treated with metastatic disease at presentation	2	1.6%
Tumor treated at outside facility with residual disease seen at our facility for tumor bed excision	15	12.4%
Treatment Timing	**126**	**100.0%**
No radiation	17	13.5%
Preoperative	74	59%
Postoperative	6	4.8%
Pre and Postoperative	29	23%
Radiation Location	**109**	**86.5%**
Community facility	38	35.8%
Tertiary center	71	64%
Radiation Technique	**109**	**86.5%**
IMRT	28	25.7%
3D-CRT	9	8%
2D-CRT	72	66.0%

PAPER 21

Soft Tissue Sarcoma Of The Extremities: The value Of Treatment At High-Volume Centers

Authors: Alexander L. Lazarides, MD[1], David Kerr, BA[2], Daniel Nussbaum, MD[3], R. Timothy Randall, BA[2], Jason Somarelli PhD[1], Dan Blazer III, MD, FACS[3], Brian Brigman, MD, PhD[1], William Eward MD, DVM[1]

Institutions: Department of Orthopedics Surgery, Duke Medical Center, Durham, NC; Duke University School of Medicine, Durham, NC; Department of General Surgery, Duke Medical Center, Durham, NC

Objective: For many types of cancer, outcomes are improved when patients receive management at treatment centers that encounter high numbers of cases annually. This correlation has been suggested to be of even greater importance in the case of less common malignancies, such as sarcoma. Indeed, existing evidence suggests that facility case volume may impact survival in soft tissue sarcoma (STS). The largest sarcoma patient registry to date is contained within the National Cancer Database (NCDB).

Purpose: Our goal was to determine the impact of facility case volume on outcomes in patients with soft tissue sarcoma of the extremities (STS-E).

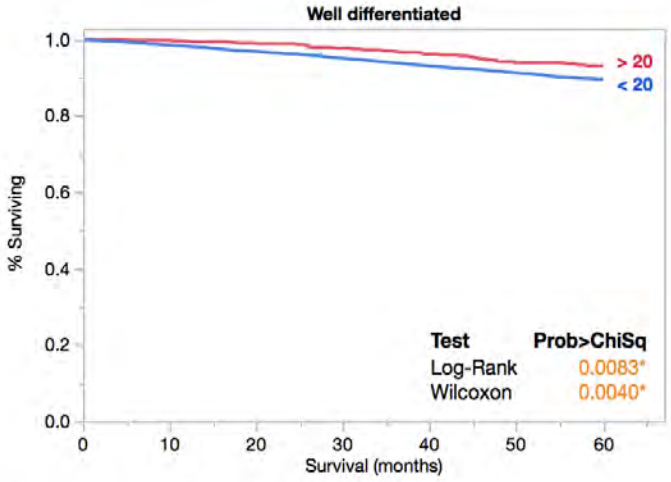
Methods: We retrospectively analyzed 25,434 STS-E patients in the NCDB from 1998 through 2012. Patients were stratified based on per year facility sarcoma volume. Univariate and multivariate analyses were used to correlate specific outcome measures with these factors. Then, long-term survival between groups was evaluated using the Kaplan-Meier (KM) method with statistical comparisons based on the log-rank test. Multiple variables were analyzed between the two groups.

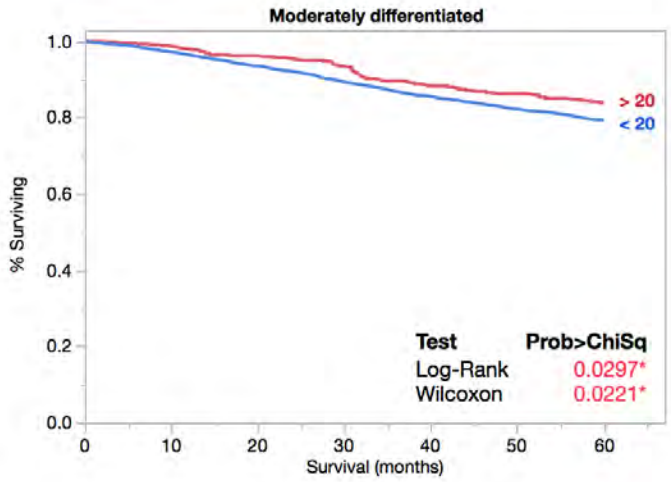
Results: Of the 25,434 patients analyzed, 3,310 were treated at high-volume centers (>20 cases annually) and 22,096 were treated at low-volume centers. Patient demographics were similar within both patient cohorts, though patients treated at high-volume centers were more likely to have larger and higher grade tumors ($p<0.001$). In a multivariate analysis, patients treated at high-volume facilities had better outcomes across several domains. They had a lower risk of mortality overall than those treated at low volume centers (risk ratio 0.792, $p<0.0001$) with five-year survival rates that were superior in patients with high grade tumors treated at high volume centers (60.1% five year survival) vs. low volume centers (54.8% five year survival, $p<0.001$). Patients treated at high-volume centers were also less likely to have positive margins ($p<0.001$) and were less likely to receive an amputations for larger intermediate-grade tumors ($p= 0.0031$). The 90 day survival was poorer at low-volume centers ($p<0.001$), and there was an estimated average five-year survival benefit of +4.5% at high-volume centers relative to their low-volume counterparts ($p<0.0001$).

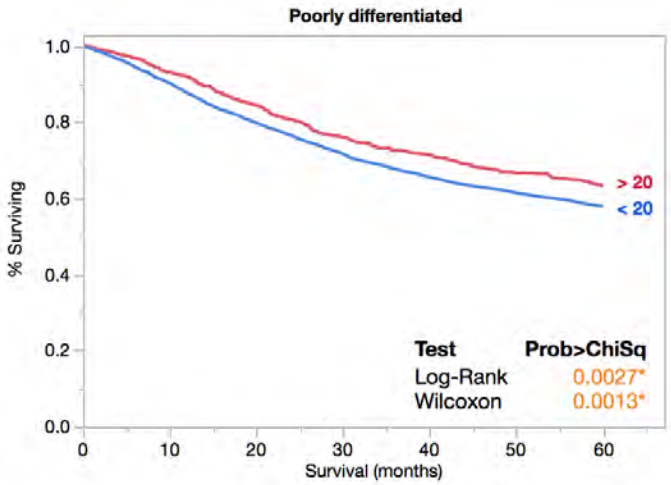
Conclusion: With the largest patient cohort to date, this database review suggests that patients with STS-E should receive treatment at high volume centers. Patients receiving treatment at high volume centers had lower rates of margin positive surgery and improved survival. Further investigation is necessary to help improve the referral of appropriate patients to the high volume sarcoma centers.

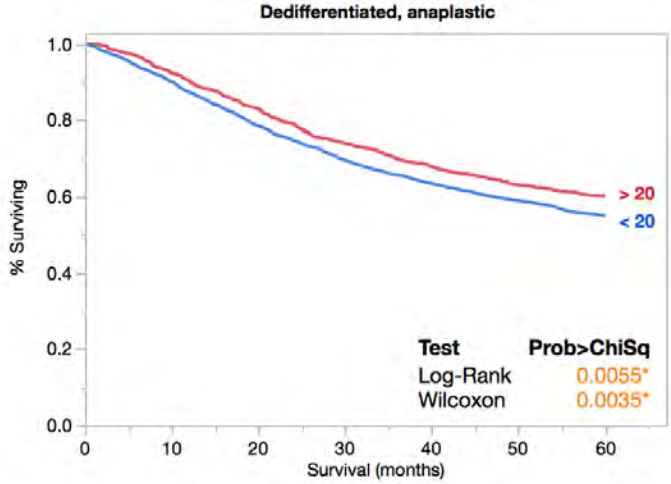
Level of Evidence: III

5-Year KM curves comparing patient survival when treated at facilities with average annual case volume greater or less than 20 per year on average, by tumor grade. Log-Rank and Wilcoxon tests for survival difference were calculated for each set of KM curves.

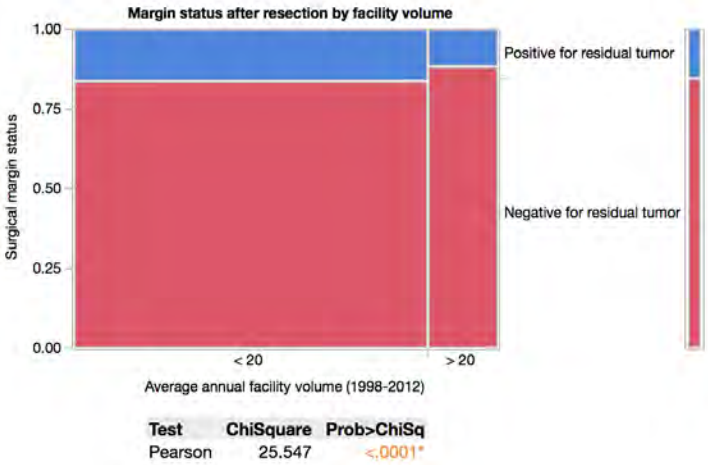


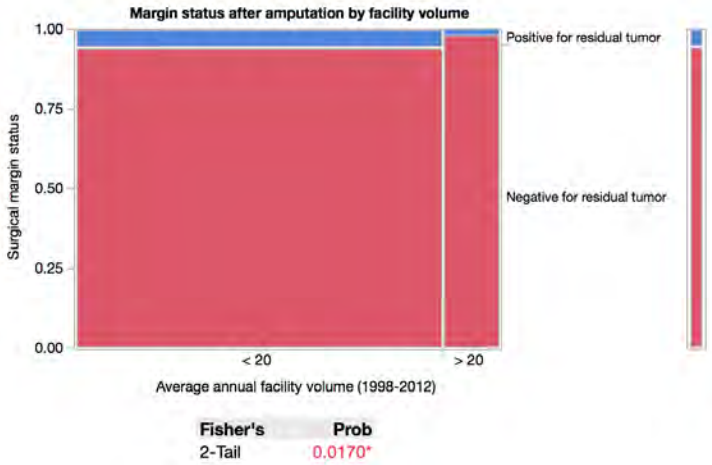






Surgical margin status by total facility volume from 1998-2012.





PAPER 22

Surgical Management of Femoral Metastases in the Era of Biologics: A Shifting Paradigm

Authors: Christina J. Gutowski, MD, MPH[1]; Benjamin Zmistowski, MD, MS[2]; Patrick J. Boland, MD[1,3], John H. Healey, MD[1,3]

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Background: A surgeon's estimate of a patient's survival and the predicted response to systemic treatment play critical roles in the decision-making regarding surgical treatment of impending or completed pathologic femoral fracture in metastatic disease. Endoprosthetic reconstruction has been shown to be more durable than open reduction internal fixation (ORIF), resulting in fewer failures and requiring fewer revision surgeries, and may be preferable in patients with an estimated survival longer than 12 months. Biologic and targeted agents offer patients with certain kidney and lung adenocarcinomas a chance at improved long-term prognosis, and this prolongation of life expectancy should be considered when treating femoral metastases.

Purpose: We investigated the relationship of biologic agents on the patient and implant survival among those with metastatic kidney and lung cancer-associated impending or completed pathologic femoral fracture. Overall survival from time of disease diagnosis and after orthopaedic surgery, the incidence of local disease progression, and implant survival in patients who received traditional cytotoxic chemotherapy were compared with those in patients who received modern biologic agents as part of their systemic treatment.

Methods: This was a retrospective review of 148 patients with metastatic lung or kidney adenocarcinoma who underwent surgery for a femoral metastasis between 2000 and 2016 at our institution. All patients received systemic treatment at some point in their disease course: in the form of traditional cytotoxic chemotherapy or a new biologic agent; those who never received systemic treatment were excluded. Patients who received a biologic agent were stratified as either "responders" or "nonresponders", as defined by response of their visceral disease to the treatment. Stable disease or regression of disease, as noted in two consecutive office notes and supported by advanced imaging studies, defined a patient as a "responder." Overall survival from diagnosis, survival from time of femoral surgery, incidence of disease progression at the site of femoral surgery, and implant failure rate were recorded for the three groups. Survival was analyzed using the Kaplan-Meier method, and the log-rank test was used to identify statistically significant differences ($p<0.05$) between patients who responded to biologics and all others.

Results: Our analysis included 148 patients with renal (n=26) and lung (n=122) cancer. Fifty-one received traditional chemotherapy only, and 97 received a biologic agent throughout their treatment course. Among the 97 treated with a biologic, 41 achieved a response (visceral metastatic disease

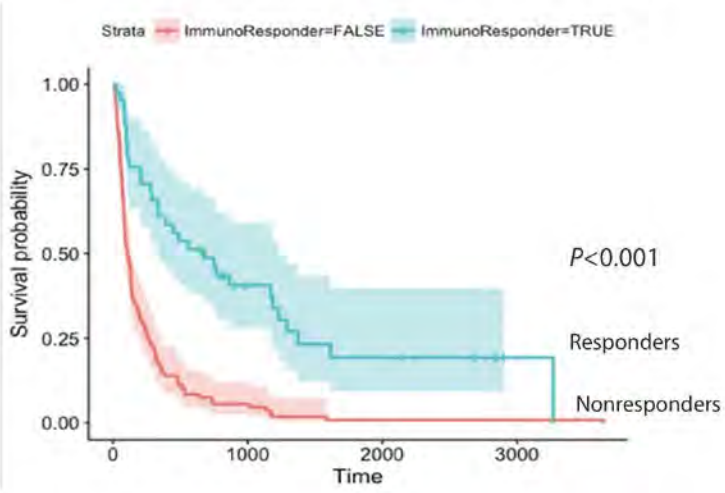
stabilized or regressed), while disease progressed in 56. Histologic and treatment parameters among responders and nonresponders are summarized in Table 1. Among the 41 responders, 3 patients who had undergone ORIF developed radiologic evidence of local disease progression around the implant and required revision after an average of 424 days after the index surgery. Among 56 patients nonresponsive to biologic therapy, 2 (3.5%) developed local progression, noted radiographically at an average of 476 days after index surgery, but none underwent revision. Among 51 patients treated with traditional chemotherapy, only 1 developed local disease progression and required revision, performed at 106 days after index surgery. Overall survival among biologic therapy responders was significantly longer than all others ($p<0.001$; Figure 1).

Conclusions: Kidney and lung cancer patients who respond to biologic treatment live longer after diagnosis and after surgical intervention for femoral lesions. There is a discordant response between visceral metastases and skeletal metastases, and it appears that while disease in visceral sites may regress, skeletal lesions may continue to progress on these biologic agents. Our patients' response status did not delay their local progression or improve the durability of their construct, as both groups demonstrated progression at nearly the same time (424 days and 476 days.) The increased life expectancy gained by responding patients introduces an increased risk for mechanical failure of fixation constructs that do not provide adequate long-term durability for patients living longer than a year. The challenge faced by the orthopaedic surgeon is to identify responders from nonresponders in the era of biologic drug development, and to ensure that the patient will not outlive his implant by performing the appropriate surgical treatment in consideration of the prognostic improvement these drugs can afford.

Table 1. Comparison of patients with and without a response to biologic agents

	Study Cohort (N=148)		
	Responders to biologic agents (n=41)	Non-responders to biologic therapy and/or chemo (n=107)	*P* value
Histology			
Lung cancer (n)	14	95	
Renal cancer(n)	27	12	
Surgical intervention			
ORIF (cephalomedullary nailing or plate/screw fixation)	13	33	
Endoprosthetic reconstruction	28	74	
Survival after diagnosis (days)	2054	704	*P*<0.001
Survival after surgery	598	243	*P*=0.009

Figure 1. Survival of biologic responders versus all others



PAPER 23

Mid-Term Results of Patients Treated With Porous Tantalum Acetabular Implants For Non-Primary Periacetabular Lesions

Authors: Matthew T. Houdek, Matthew P. Abdel, Peter S. Rose, David G. Lewallen, Franklin H Sim

Institution: Department of Orthopedic Surgery, Mayo Clinic, Rochester, MN

Introduction: The pelvis and acetabulum are common locations for the development of metastatic disease. Due to the mechanical forces transmitted through the hip, patients can have substantial pain and disability. Surgical treatment requires a reconstruction that restores mechanical stability of the hip, while providing pain control and allowing for immediate weight bearing. Historically, the Harrington reconstruction was the primary treatment option for patients with periacetabular neoplastic disease, and transmitted the load of the weak acetabulum to the stronger, intact proximal pelvis. Although these reconstructions have provided excellent short-term outcomes, there are concerns with longer follow-up the cemented reconstructions may fail and an implant which provides bony ingrowth is thought to be superior in terms of potential implant survival. We previously reported the initial use of porous tantalum shells to reconstruct non-primary neoplastic lesion of the acetabulum, with no cases of acetabular component revision at 56 months of follow-up.

Purpose: The purpose of this study is to investigate the mid-term follow-up of the use of tantalum acetabular components (1) overall implant survival; (2) rates of complications and reoperation; and (3) patient function.

Method: Fifty-eight patients (32 females, 26 males) were treated using a tantalum acetabular component and total hip arthroplasty (THA) to reconstruct a non-primary neoplastic process between 2001 and 2014. The mean age and body mass index (BMI) were 62 years and 28 kg/m2, respectively. The most common diagnosis was metastatic disease (n=29). The patients' medical records and radiographs were reviewed to assess Harris hip scores and radiographic fixation. The mean follow-up for surviving patients was 6 years.

At the time of surgery, the most common diagnosis were metastatic disease (n=29; 50%) and myeloma (n=20; 34%) (Table 1). The Eastern Cooperative Oncology Group (ECOG) preoperative performance status were 0 (n=2; 4%), 1 (n=21; 36%), 2 (n=20; 34%), 3 (n=12; 21%), and 4 (n=3; 5%). Acetabular deficiencies included Harrington Class I (n=25; 46%), Class II (n=7; 13%), and Class III (n=22; 41%). For the revision THA's (n=4, 7%), the classifications

were AAOS Type II (n=2; 50%%), Type III (n=1; 25%) and Type IV (n=1; 25%). Prior to the surgical procedure, 43 (74%) patients received neoadjuvant radiotherapy.

The reconstruction was performed with a tantalum shell alone (n=21; 36%), tantalum shell with augments (n=6; 10%), tantalum cup-cage (n=23; 40%), and tantalum cup-cage with augments (n=8; 14%).

Results: Over the course of the study, none of the acetabular tantalum components were revised. Two patients had failure of the surgical hardware (pelvic reconstruction plate in one patient and acetabular screw in one patient). However, neither required revision. Both these patients had a history of a non-union of a pelvic discontinuity in the setting of preoperative radiotherapy.

In addition, one patient underwent conversion to a constrained acetabular insert due to recurrent dislocations. At the time of revision, the acetabular shell was well fixed and in acceptable position

Following the acetabular reconstruction, 13 patients had an incomplete radiolucent line apparent on their immediate postoperative radiograph. There were no complete radiolucent lines. Five of these resolve by the patients most recent follow-up radiographs. Two patients had progression of the radiolucent line; however these patients had disease progression around the hip.

Prior to the reconstruction, the mean Harris Hip Score was 37 (range, 4-77), which significantly improved (p=0.0001) to 72 (range, 23-93) at last follow-up. Patients with metastatic disease (mean 66±3) had significantly worse (p=0.01) postoperative HHS compared to patients with myeloma (mean 76±4) and lymphoma (mean 83±3).

Conclusion In patients with periacetabular metastatic diseases and the need for total hip arthroplasty, acetabular reconstruction utilizing a highly porous tantalum shell provides patients with a durable means of reconstruction, with no cases of component failure at mid-term follow-up.

Table 1: Patient Demographics and Function

Demographics	Number of Patients (% of Patients)
Males	26 (45%)
Females	32 (55%)
Mean Age	62 (range 22-88) Years
Mean Body Mass Index (BMI)	28.1(range 17.2-48.8) kg/m^2
Preoperative Radiotherapy	43 (74%)
Tumor Pathology	
Metastatic Disease	29 (50%)
Breast	9 (16%)
Prostate	6 (10%)
Lung	2 (3%)
Other	12 (21%)
Myeloma	20 (34%)

Lymphoma	14 (24%)
Langerhans Histiocytosis	1 (2%)
Rosai-Dorfman Syndrome	1 (2%)
Other: Carcinoma Unknown Primary (n=1), Chordoma (n=1), Cystic Adenocarcinoma (n=1), Leiomyosarcoma (n=1), Melanoma (n=1), Ovarian Carcinoma (n=1), Pheochromocytoma (n=1), Rectal Adenocarcinoma (n=1), Renal (n=1), Urothelial (n=1)	

PAPER 24

What are the short term costs associated with endoprosthetic reconstruction versus surgical fixation of bone metastases from renal cell carcinoma?

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Background: In patients with pathologic or impending fractures from bone metastases, orthopaedic surgeons are faced with the question of whether to stabilize the bone versus replace the bone, or segment of bone, in question with an endoprosthesis. While outcomes of both methods have been widely reported, the costs associated with each method of surgical intervention within the United States are less well known. This is of particular interest in a healthcare climate focused on reducing cost, especially at the end of life.

Questions/Purposes: (1) What are the short term (90 day) costs to the hospital and payer charges associated with endoprosthetic reconstruction versus surgical fixation for bone metastases from renal cell carcinoma? (2) Is there a statistically significant difference in costs/charges between these two methods of surgical intervention?

Patients and Methods: After obtaining institutional review board (IRB) approval, the orthopaedic oncology database of two affiliated tertiary care centers was queried for adult patients with appendicular bone metastases from renal cell carcinoma from 2006 to 2015. Data on costs incurred by the hospital, charges submitted, and payments received were requested from the hospitals' billing departments for each patient over a 90 day period beginning from the date of surgery. These data included all costs associated with the patient's inpatient hospitalization (including operative & anesthetic costs), any subsequent hospitalizations/surgeries, and outpatient care. Costs associated with post hospitalization care (such as rehabilitation) were not available.

Demographic data, location of the bone metastasis, and the surgical technique (fixation versus endoprosthesis) were recorded.

Statistical analysis was carried out in Microsoft Excel. Mean and standard deviations were calculated for patients grouped by surgical technique and further stratified by anatomic region (acetabulum/pelvis, distal femur, femoral shaft, humeral shaft, and proximal humerus). Comparison of means was performed via two-tailed two sample t test with significance level of $P < 0.05$.

Results: 51 patients with 57 surgical episodes were identified; 6 patients had 2 surgical procedures separated by more than 90 days. The distribution of surgical locations was the proximal femur in 16 surgeries; humeral shaft in 12; femoral shaft in 10; proximal humerus in 7; pelvis/acetabulum in 6; forearm in 3; and distal femur in 3.

Endoprosthetic reconstruction was performed in 29 cases (51%) while surgical fixation was undertaken in 28 (49%). Methods of surgical fixation included plates, intramedullary/cephalomedullary nails, and Steinmann pins. Endoprosthetic reconstruction was performed in 10 proximal femora, 6 proximal humeri, 4 acetabulae, 3 distal femora, 2 femoral shafts, and 1 humeral shaft.

Mean cost, charge, and payment for all patients who underwent surgical fixation procedures were $36,822 (SD = $20,918), $119,909 (SD = $64,141), and $40,903 (SD = $30,741), respectively. Mean cost, charge, and payment for all patients who underwent endoprosthetic reconstruction were $65,620 (SD = $37,255), $218,763 (SD = $114,286), and $82,711 (SD = $76,951), respectively. The difference in the mean values for cost, charges submitted, and payments received between surgical fixation and endoprosthetic were statistically significant when the data from all anatomic regions were analyzed as a whole.

Conclusions: In patients with bone metastases from renal cell carcinoma, surgical fixation is less expensive than endoprosthetic reconstruction in the first 90 days in terms of costs incurred, charges submitted, and payments received. For patients with widely metastatic disease and limited life expectancy, surgical fixation is clearly the more cost effective method for addressing pathologic/impending fractures. Patients with solitary or oligometastatic disease, however, are known to have improved survival with resection involving negative margins; thus the increased short term cost of resection and endoprosthetic reconstruction may be justified by better survival in this subgroup of patients. Future directions include following the costs of care associated with this patient cohort to the time of death to evaluate whether endoprosthetic reconstruction becomes more cost effective in the long term and gathering data on more patients to stratify the cost data by extent of metastatic disease.

Table 1: Cost, Charge, and Payment Data for Internal Fixation (ORIF) versus Endoprosthetic Reconstruction (EPR)

	Cost			Charge			Payment		
	ORIF	**EPR**	**p value**	**ORIF**	**EPR**	**p value**	**ORIF**	**EPR**	**p value**
Acetabulum/Pelvis	$68,503	$69,301	0.9855	$229,664	$211,390	0.8863	$54,889	$37,921	0.5245
Proximal Femur	$26,804	$67,903	0.0697	$96,952	$218,480	0.0900	$46,801	$78,104	0.4493
Femoral Shaft	$42,965	$69,069	0.1818	$125,908	$189,073	0.2499	$46,034	$85,265	0.3234
OVERALL	$36,822	$65,620	0.0005	$119,909	$218,763	0.0001	$40,824	$82,711	0.0074

PAPER 25

Critical Analysis Of Prophylactic Stabilization For Osseous Metastatic Disease In Long Bones With Low Mirels Scores

Authors: Adam S. Levin, MD; Brett A. Shannon, MD; Carol D. Morris, MD. Jonathan A. Forsberger, MD

Institution: John Hopkins University

Background: When considering the appropriateness of prophylactic stabilization of a long bone in the setting of osseous metastasis, multiple clinical factors must be considered. The Mirels scoring system has been proposed as a model for predicting the risk of pathologic fracture, though this system is not always ideal for each clinical scenario. In the initial study by Mirels, for example, the location of the lesion was itself not an individual predictor of the risk of pathologic fracture following radiation for a metastatic lesion. Furthermore, consideration of a patient's estimated survival, rehabilitation needs, and anticipated additional treatments may all influence the decision as to whether to prophylactically operate on a patient with osseous metastases – none of which are otherwise factored into the scoring system.

Purpose: The authors wish to evaluate 1) the association between those patients deemed clinically appropriate for prophylactic stabilization for osseous metastatic disease and the respective Mirels scores of the affected long bone. In addition, we also wanted to review 2) the clinical indications for prophylactic operative intervention in those long bones whose score was 8 or less.

Methods: After Institutional Review Board approval, a retrospective review of the Orthopaedic Oncology database at Johns Hopkins University was used to identify all patients treated with prophylactic stabilization of a long bone for osseous metastasis by the Orthopaedic Oncology division at Johns Hopkins Hospital over a two year period from 2014 to 2016. In total, 43 patients met the inclusion criteria, and were evaluated for age, sex, location of the lesion, size of the lesion, matrix properties, and the pattern of pain, so that a Mirels score could be calculated. Chart abstraction as to additional factors leading to the decision to operate was recorded for each patient as well.

Results: A total of 47 long bones in 43 patients underwent prophylactic stabilization by the Orthopaedic Oncology division over the two-year period. Of those, 9 (19%) were calculated to have a Mirels score of 8 or less (Figure 1). For those who underwent operative treatment, there were multiple factors that were identified as reasons for the need to operatively stabilize, including a cortically-based lesion (4 patients) or pain that was refractory to all other modalities (3 patients). The three patients treated with humeral intramedullary nail fixation with Mirels

scores of 8 or less all had lower extremity lesions that required stabilization as well, with concerns over the need for increased weightbearing of the humerus during rehabilitation following lower extremity surgery (Table 1).

Of those nine patients treated with scores of 8 or less, six have maintained complete pain relief at that site of concern, two had progressive improvement in function and pain control at their most recent followup, and one experienced transient relief until a subsequent trauma resulted in an incomplete fracture around the prophylactic intramedullary nail 13 months postoperatively. Three patients have since died of disease under hospice care with sustained pain relief (range 1-4 months), two of whom underwent subsequent stabilization of other pathologic fractures. The remaining six patients are all alive at a median of 15 months (range 5-30 months).

Conclusion: The current analysis reflects the complexities of the decision to prophylactically stabilize. The Mirels scoring system was not intended to be a strict analog determinant of the need for operative treatment for osseous metastases, but rather a prediction algorithm. This study evaluates some of the factors involved in determining the need for stabilization in those for whom the Mirels score would indicate otherwise.

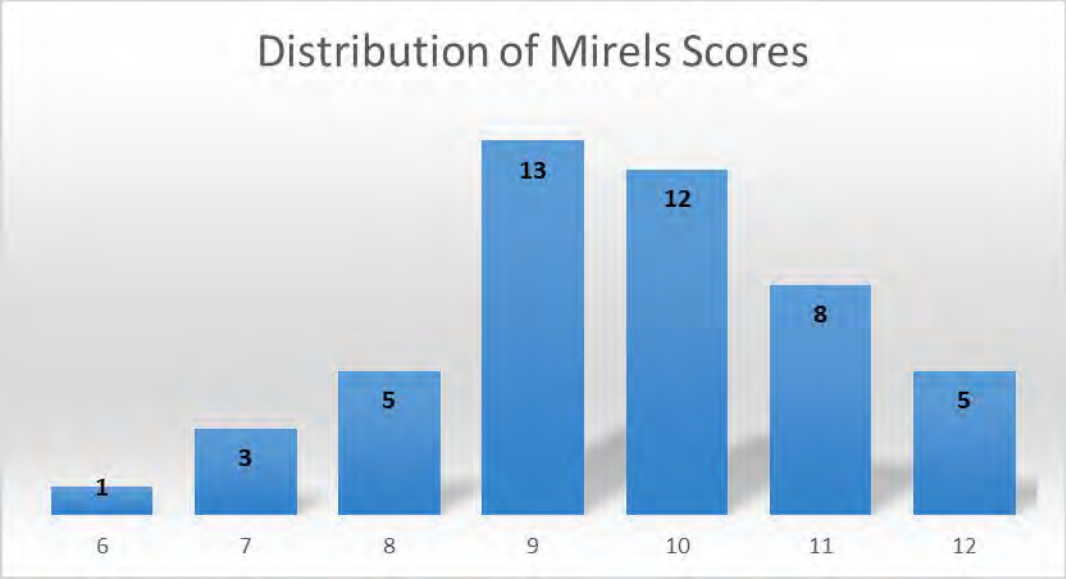

Figure 1: The Mirels score was calculated for each prophylactically stabilized long bone in the setting of osseous metastasis. The distribution of the Mirels scores for those undergoing operative treatment is shown.

Patient	Matrix	Site	Pain	Size	Rehab of other bone	Other lesion in the same bone	Cortical erosion	Failure of conservative measures	Mirels	Treatment
1	Lytic	UE	Mild	2/3	+	+	+	-	6	IM Nail R humerus
2	Lytic	UE	Mild	2/3	+	-	-	-	7	IM Nail R humerus
3	Mixed	LE	Moderate	1/3	-	-	+	+	7	IM Nail tibia
4	Mixed	LE	Moderate	1/3	-	-	+	-	7	IM Nail R femur
5	Sclerotic	Peritroch	Moderate	2/3	-	-	-	+	8	IM Nail L femur
6	Lytic	UE	Moderate	2/3	+	-	-	-	8	IM Nail L humerus
7	Lytic	LE	Mild	2/3	-	-	+	-	8	IM Nail L femur
8	Lytic	LE	Mild	2/3	-	-	-	-	8	IM Nail R femur
9	Sclerotic	Peritroch	Moderate	2/3	-	-	-	+	8	IM Nail R femur

Table 1: Of the patients treated with prophylactic stabilization with Mirels scores of 8 or less, additional clinical factors that played into the decision to operate were reviewed.

PAPER 26

Clinical characteristics of acral metastases

Authors: Aziz K, Abiad J, Levin A, McCarthy E, Morris C.

Background: Metastatic skeletal disease is the most common form of oncologic disease encountered in orthopaedic oncology, and osseous metastases develop in up to 30% of patients with metastatic disease. Metastases to the hand or foot, known as acrometastases, is a rare occurrence, representing 0.007 to 0.3% of all cancer patients per previous reviews. Scant literature exists within the last three decades regarding large institutional experience with acrometastases, over which time advances in oncologic management and treatment have been mirrored by improvements in prognosis and life expectancies of cancer patients. As a result, metastatic skeletal disease is becoming an increasingly bigger component of the management of an oncological patient, as reflected by the steady increase of cases of acrometastases reported in literature. This highlights the importance of describing the demographics and pathology of acrometastatic carcinoma in the current era, in order to better inform clinicians and patients, and potentially to avoid diagnostic delay.

Purpose: The purpose of the current study is to characterize the incidence, pathology, and demographics of patients with skeletal acrometastasis at a single comprehensive cancer center over a period of 26 years.

Patients and Methods: The records of all patients with histologically proven oncologic disease that were evaluated and treated by the oncology service at Johns Hopkins Hospital were retrospectively reviewed. From this group, patients with osseous metastases were identified using radiology, oncology, or orthopaedic record abstraction. Following Institutional Review Board approval for this retrospective review, data was collected, including demographic data, pathology of primary lesion, location of acrometastasis, primary treatment, and presence of other osseous lesions. The records of all patients from 1990 to 2016 were included in this study. Patients with metastatic disease to the hands and feet were identified and demographic and treatment data were analyzed when available. We excluded patients with peri-articular disease in the distal tibia/fibula and distal radius/ulna from analysis.

Results: Of the 19,559 patients in the oncologic databases at our institution, 2,233 were identified to have definitive osseous metastases (11.4%). Of this subset, 27 patients were identified to have acrometastases (0.14% of total oncologic patients, or 1.2% of patients with osseous metastases). The most common primary cancers that progressed to

acrometastases in declining order was lung carcinoma (33.3% of acrometastases), with renal cell carcinoma (14.8% of acrometastases), and prostate carcinoma (14.8% of acrometastases) being the second most common. Acrometastatic disease was more common in men (63.0%, 17/27). The average age of a patient diagnosed with acrometastatic disease was 59 (range 16-73 year of age). More patients in our series had lower extremity acrometastatic disease (15/27) compared to upper extremity acrometastatic disease (13/27) – with one patient having both upper and lower extremity acrometastatic disease. In patients with lower extremity acrometastases, 46.7% (7/15) were to the hindfoot, 40% (6/15) were to the forefoot, and 13.3% (2/15) were to the midfoot. Of upper extremity acrometastases, 53.8% (7/13) were to the metacarpals, 38.5% (5/13) were to the phalanges, and 7.7% (1/13) were to the carpal bones. Overall, 3 patients presented with an acral metastatic lesion as the first sign of an occult malignancy. Of the 27 patients in our series, 21 were followed up extensively, 12 of whom were found to have osseous metastases in the absence of visceral metastases. Based on available treatment data, the most common form of treatment for acrometastases was resection or curettage followed by radiation.

Conclusions: Despite significant advances in management of cancer and shifting patterns of metastatic disease over the last 30 years, there is little change in the incidence of diagnosed acrometastatic disease. Lung carcinoma remains the most common primary that may develop acrometastases. Interestingly, our series shows an almost equal rate of upper and lower extremity acrometastases, which is different than what has been previously reported. Additionally, while metastates to the carpal row are quite rare – metastatic disease to the hindfoot is the most common form of acrometastatic disease to the lower extremity. Further study is needed to identify possible biologic factors that may predispose patients to acrometastases.

Figure 1:
Diagram demonstrating the relative distribution of acrometastases in the hand and foot.

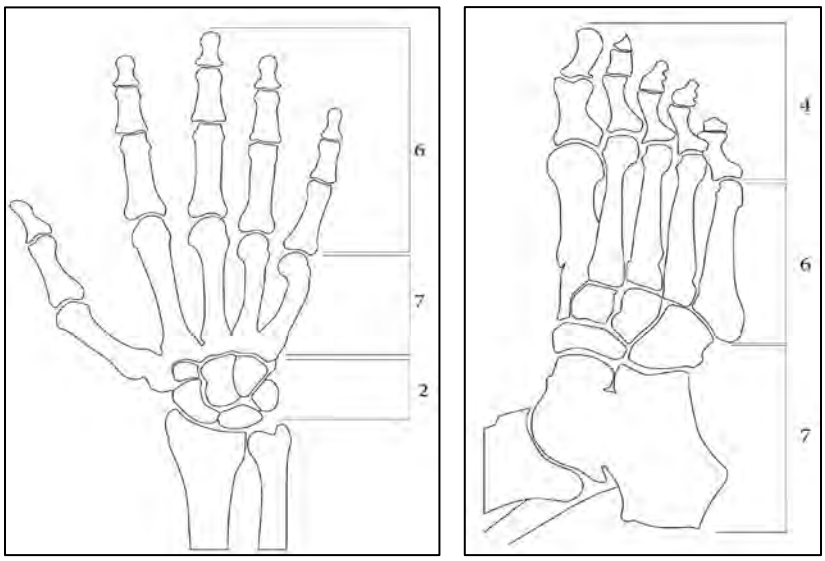

Table 1: Local and distant treatment modalities utilized for acrometastases

Management	Number
None	3
Radiation	4
Chemo	0
Resection/Curretage	7
Amputation	2
Zometa/denosomab	1
Chemo + Radio	0
Radio + Excision	3
Radio + Amputation	1
Not documented	7

PAPER 27

Operative Treatment Of Non-Primary Tumors Of The Acetabulum: Is A New Classification System Needed?

Authors: Matthew T. Houdek MD, Anthony M. Griffin MS, Peter C. Ferguson MD, Jay S. Wunder MD

Background: The periacetabular region of the hip is one of the most common locations for the development of bony metastatic disease. Historically these oncologic defects have been classified and reconstructed based on the system by Harrington. Although this system is routinely used, a majority of defects do not fit this classification.

Purpose: The purpose of this series was to report our institutions outcome of the treatment of periacetabular metastatic disease using this type of reconstruction and propose a modification to this system which has the potential to impact outcome.

Methods: A retrospective review identified 77 consecutive patients undergoing acetabular reconstruction for a metastatic tumor. Mean age was 60 years at the time of the surgery with 44% being male. The most common preoperative ECOG rating was 3 (n=28).

The reconstructive procedures were performed by removing all gross accessible tumor in the acetabulum by curettage and then the acetabular deficiency was assessed. Acetabular deficiencies were then classified based on the classic Harrington Classification. This included Class 1: contained acetabular defects, but intact lateral cortices, and intact medial and superior walls (n=18); Class 2: intact lateral cortices, posterior and superior wall, with a deficient medial wall (n=8); Class 3: deficient lateral cortices, with deficient anterior and posterior column and superior and medial wall (n=15). Our modification is based on our observation that following tumor curettage, a portion of the medial wall is often deficient, but in combination with a deficient anterior column and intact posterior column (Class 2A, n=11); or deficient posterior column and intact anterior column (Class 2B, n=25). In patients with Class 2B and Class 3 defects, 19 patients had disease extension into the ischium. At the time of surgery 48 patients had a pathologic acetabular fracture.

This reconstruction technique was supplemented with Steinmann pins alone (n=11), a roof-ring (Zimmer/Biomet) and multiple screws (n=27); roof-ring (Zimmer/Biomet), multiple screws and Steinmann pins (n=18); antiprotrusion cage (Zimmer/Biomet) and multiple screws (n=13); and antiprotrusion cage (Zimmer/Biomet), multiple screws, and Steinmann pins (n=8). If screws or Steinmann pins were used in the case, the mean number of screws and Steinmann pins were 5

(range 1-13) and 7 (range 3-10). The mean outer diameter of the roof ring or reconstructive cage was 52 mm (range 44-64 mm). Patients with ischial extension were more likely to be reconstructed with either an antiprotrusion cage or Steinmann pins (OR 3.50, P=0.09).Prior to surgery, 28 patients received radiation to the acetabulum. The mean follow-up for surviving patients was 3 years (1-12 years).

Results: The mean 2-, 5-, and 10-year overall survival was 35%, 8%, and 4%. Nine patients required revision of the acetabulum. Indications included aseptic loosening without recurrence (n=2), disease progression leading to loosening (n=2), dislocation (n=2), deep infection (n=2) acetabular fracture (n=1). Patients with a 2B deficiency whom were not reconstructed with Steinmann pins or an antiprotrusion cage were at increased risk of failure (P=0.04). Patients had a significant improvement in functional status (P<0.0001).

Conclusion: Following acetabular reconstruction for metastatic disease, patients had a significant improvement in function. If there is a combined posterior column and wall deficiency it should be reconstructed with Steinman pins or a reconstruction cage. Following reconstruction patients have reliable functional improvement.

PAPER 28

The Impacts of Diagnosis and Surgical Acuity on Patient-Reported Outcomes using PROMIS in Operative Patients with Malignant and Benign Tumors as Compared to Orthopaedic Trauma Patients and the U.S. Population.

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Institution: University of Florida, Department of Orthopaedic Surgery and Rehabilitation, 3450 Hull Road, Gainesville, Florida, 32607

Background: Patient-reported outcome measures are increasingly important in patient care and health systems. The NIH-funded Patient Reported Outcomes Measurement Information System (PROMIS) improves our ability to capture patient-reported outcomes in a standardized fashion that permits comparisons across disease-states and ages by normalizing the results to a common mean. The quality of life modalities captured by this instrument include physical health, social health, and mental health. We provide the first comparison of Orthopaedic Onology and Orthopaedic Trauma patients using these instruments during the first postoperative year.

Questions/Purpose: (1) Are patient-reported outcomes impacted by diagnosis? (2) Are patient-reported outcomes impacts by surgical acuity? (3) Are patient-reported outcomes among patients 6-12 months from surgery different than the U.S. population norm?

Patients and Methods: As a standard of care, we routinely collect PROMIS questionnaires for all adult patient visits with the Division of Orthopaedic Oncology; this includes oncology, trauma, and general orthopaedic patients. The patients electronically answer the questionnaires at the start of each routinely scheduled clinic visit and their responses are saved to their EPIC profile as a patient questionnaire. The PROMIS surveys are scored using T- scores that are normalized and calibrated to a diverse sample of 21,133 subjects of both healthy and sick patients in a United States patient population. The normalized mean in the PROMIS surveys is 50 with a SD of 10 and higher scores indicate more of the metric being studied; for example, a higher anxiety score indicates more anxiety and a higher mobility score indicates more mobility. Survey data are scored according to the PROMIS Scoring Manuals. We retrospectively collected 3 months of prospectively collected PROMIS data from September 1st to December 31st, 2016 and performed a chart review for demographic and treatment variables. For patients who completed serial questionnaires, we selected the first entry to limit bias. Of 604 adult patients who completed the surveys, 110 patients within 12 months of surgery with

nonmetastatic oncology and traumatic diagnoses were identified and used for this analysis. Patients were divided by diagnosis into benign (n=24), malignant (n=34), and trauma (n=51). Further, these groups were stratified by surgical acuity: 0-6 months and 6-12 months from any surgical intervention. Multifactorial analysis of variance were used to conduct statistical analyses for each PROMIS modality. We then assessed whether scores of the diagnostic groups differed from the U.S. general population norm by one-sample signed rank test.

Results: There were no differences in demographic variables between groups. The average age of the cohort was 55 +/- 18 years, and 51% was male. Patients with trauma diagnoses who were 6-12 months from surgery had higher pain scores on an 10-point scale (p=0.04). Compared to those 6-12 months from surgery, patients within 6 months of surgery had lower (worse) Physical Function T-scores (mean 37, 95% CI 35-38%, p=0.04) and worse Ability to Participate T-scores (mean 44, 95% CI 40-45%, p=0.02). These differences were not dependent on diagnosis type. Patients with malignant diagnoses had lower (better) Pain Interference T-scores (mean 55, 95% CI 52-59%), than patients with traumatic diagnoses (mean 63, 95% CI 59-68%) with a p-value of 0.04. For each diagnosis group, five of the seven PROMIS modality T-scores did not differ significantly from the generalized U.S. population norm. Patients with malignant and traumatic diagnoses had worse Physical Function T-scores than the U.S. population norm of 50 (p=0.04 and p=0.01, respectively). Patients with benign and traumatic disease had worse Pain Interference T-scores (p=0.02 and p=0.01, respectively).

Conclusions: We provide normative data on patient-reported outcomes for patients with benign and malignant musculoskeletal pathologies during the first postoperative year and compared these data to patients with traumatic diagnoses and to the general U.S. population standardized median for PROMIS measures. All diagnosis groups improved over time but patients with malignant diseases tended to have better scores than those with benign or traumatic diagnoses.

PAPER 29

A Comparison of Limb Salvage versus Amputation for Non-Metastatic Sarcomas using PROMIS Outcomes

Authors: Benjamin Wilke MD; Anna Cooper MD; Mark Scarborough MD; Parker Gibbs MD; Andre Spiguel MD*

Institution: Division of Orthopaedic Oncology, University of Florida

Background: The Patient Reported Outcomes Measurement Information System (PROMIS) is a United States (U.S) National Institute of Health – funded scoring tool that normalizes data to a reference population consisting of a subset of the United States general population. This allows comparisons between rare conditions, such as sarcomas, to more common ailments or even the U.S. general population.

Purpose: Our purpose in this study was to compare PROMIS outcomes between patients who underwent limb salvage and amputative surgeries. Additionally, we compared these results to the U.S. general population

Methods: We included 138 patients in the evaluation and divided these into those who had undergone a limb salvage (114) or an amputative procedure (24) patients. Patients were further divided into early (1-11 months) and late (12+ months) follow up.

Results: We evaluated 7 PROMIS health domains and found a statistically significantly higher Physical Function score in the limb salvage group compared to the amputative cohort. Additionally, we found significant improvements in the Physical Function, Ability to Participate, and Pain Interference domains as patients recovered from surgery (**Figure 1**). When compared to the U.S. general population, we found statistically significant better scores in the emotional health domains (Sleep Disturbance, Fatigue, and Depression) in the limb salvage group compared to the U.S. population (**Figure 2**).

Conclusion: We found several improvements in PROMIS health domains as the patients progressed further from surgery. Additionally, patients who underwent limb salvage were found to have significantly improved scores in the Physical Function domain when compared to the amputative cohort, as well as improved scores in the emotional health domains when compared to the U.S. general population.

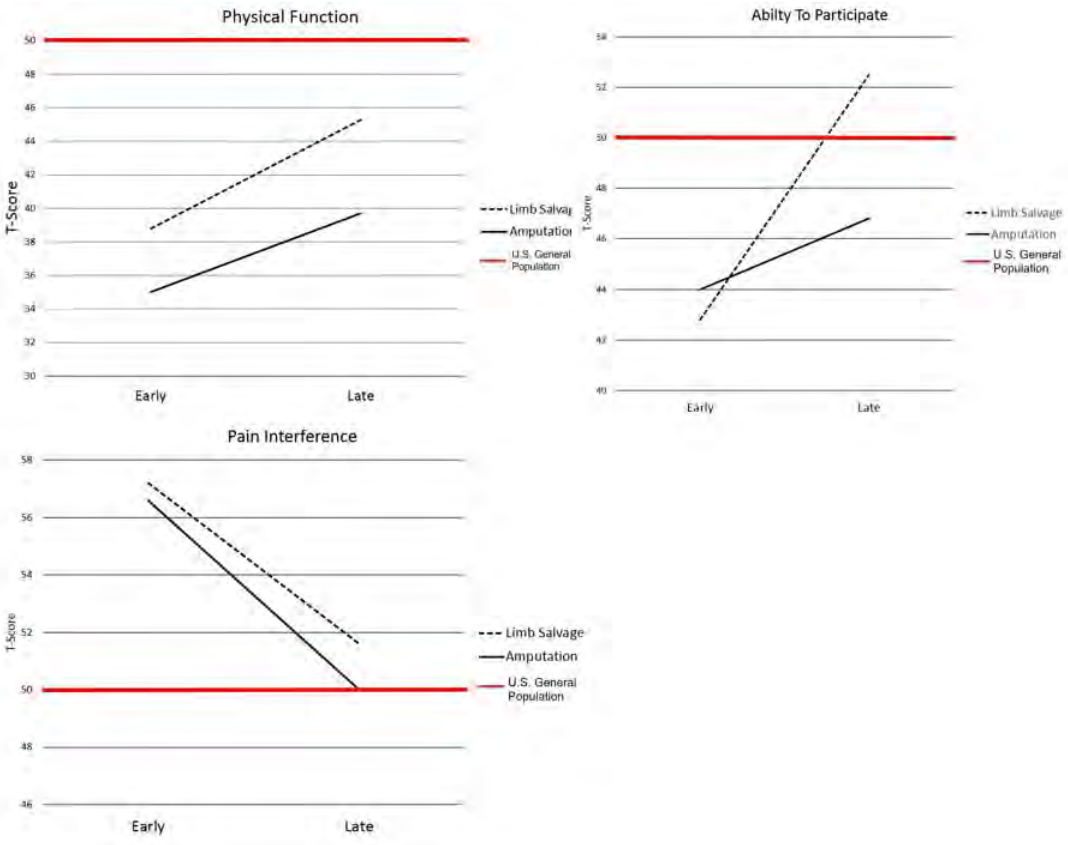

Figure 1: Comparison of limb salvage versus amputative outcomes. Early is as < 12 months postoperatively and late is defined as > 12 months postoperatively.

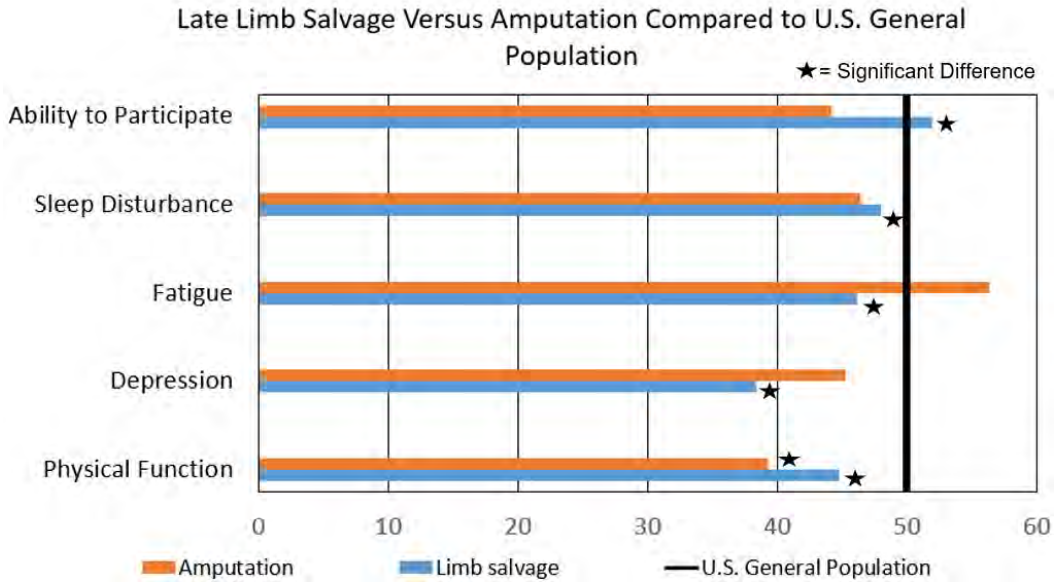

Figure 2: Comparison of late limb salvage and amputation compared to the United States general population.

PAPER 30

Concurrent Validity and Responsiveness of the Timed Up and Go Test (TUG) and the 10 Meter Walk Test (10MWT) in Orthopaedic Oncology Patients

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Institution: MD Anderson Cancer Center, Houston, Texas

Background: Surgeons routinely use outcome measures to assess patients' function in order to determine the clinical effectiveness of operative interventions. Many measures capture similar functional abilities, a redundant process which burdens the patients and clinicians. It is important, therefore, to identify tools with high concurrent validity and select the one that is most efficient and responsive to changes for the patient population being assessed. The Timed Up and Go Test (TUG)[1] and the 10 Meter Walk Test (10MWT)[2] have been reported to have a high correlation (r=0.89) in patients with spinal cord injury.[3] However, our literature review did not identify articles comparing the TUG and 10MWT in a sample of orthopaedic cancer patients.

Purpose: 1) To determine the concurrent validity of the TUG and 10MWT for orthopaedic oncology patients treated with lower extremity or pelvic/spine surgery; and 2) to determine if either test demonstrates a higher degree of responsiveness (i.e., detecting change over time) in our patients. The goal was to decrease outcome measurement burden and redundancy for timed gait assessments.

Patients and Methods: A retrospective study to evaluate prospectively obtained functional outcome data was approved by our Institutional Review Board. Thirty-six patients who underwent orthopaedic oncology surgery from a single surgeon between May 2015 and Oct 2016 were included in this study. All patients were tested by the same physical therapist using a permanently marked, standardized distance in the same location for each test for a total of 61 pre-operative and follow-up visits. Each test was performed twice for all clinical visits.

The patient reported physical health question from the PROMIS Global Health tool was used to evaluate responsiveness of the objective timed walk tests. We compared the patient reported response on each clinic visit and coded this score as (1) better or no change, or (0) worse for each clinic interval. For instance, if a patient at the pre-op visit reported his physical health was "fair" and then at his 3 month follow up visit reported his physical health was "good" his interval response was coded a (1).

Results: The correlation between trial 1 and trial 2 of the TUG was r=.923 and for the 10MWT was r=.966 using a similarity matrix. Given the low variability between trials, the average values

were used to test validity. The concurrent validity (Pearson correlation) of the averaged TUG and 10MWT in orthopaedic oncology patients was high r=0.85 (Figure 1).

A receiver operating characteristic (ROC) curve was utilized to determine responsiveness of each functional outcome measure in relation to patient reported outcomes of physical health. Nineteen patients with 33 time points were include in the ROC analysis utilizing the dichotomized score for change in patient reported outcome. The TUG was more responsive to functional change for our patients than the 10MWT as demonstrated by a greater area under the curve (AUC) (Figure 2).

Conclusions: The TUG and 10MWT have high concurrent validity for orthopaedic oncology patients treated with lower extremity or spine/pelvic surgery. The TUG demonstrated a higher degree of responsiveness to patient reported physical function changes post-operatively than the 10MWT. Thus, the TUG should be used as a single measure of gait speed for orthopaedic cancer patients in order to reduce measurement burden and outcome data redundancy.

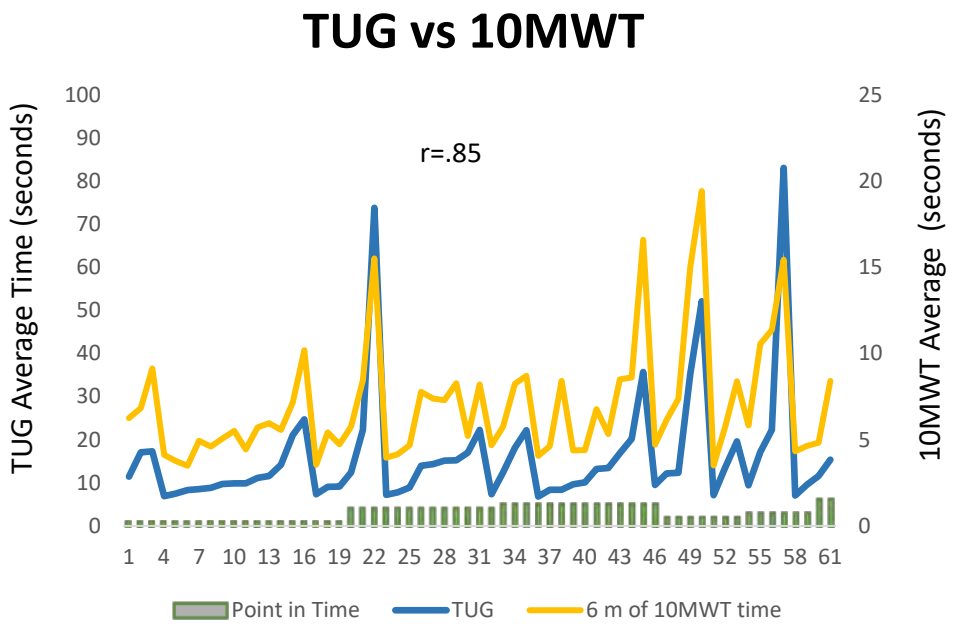

Figure 1: This graph illustrates the Timed Up and Go (TUG) and 10 meter walk test (10MWT) at the same point in time for the same patient. It can be seen from this graph (comprised of 36 patients for a total of 61 time points) that the TUG and 10MWT demonstrated similar patterns for timed gait for individual patients with a correlation of r=0.85.

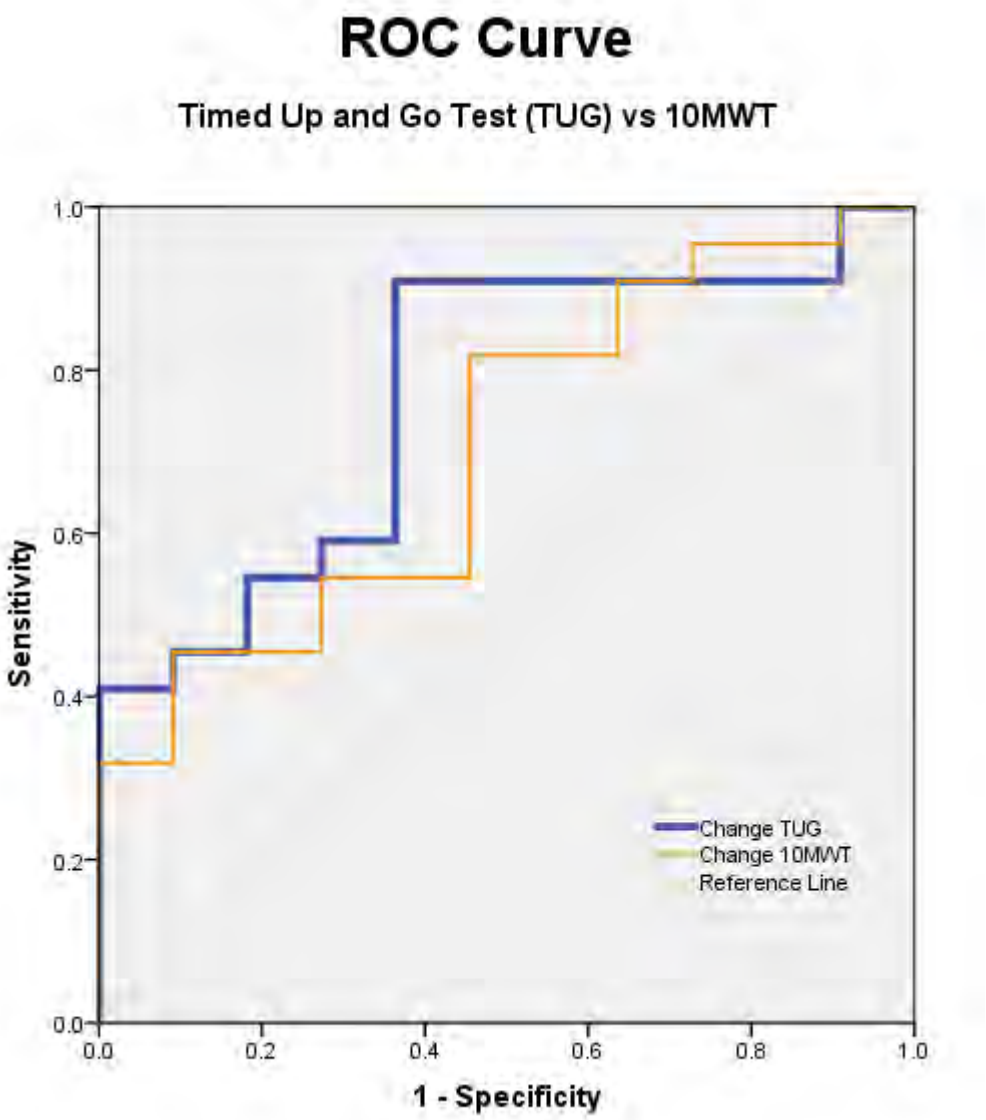

Figure 2: The Receiver Operating Characteristic (ROC) curve was drawn using SPSS 23 using data from nineteen patients (33 time points) by a nonparametric method. The TUG was more responsive to functional change for our patients than the 10MWT as demonstrated by a greater area under the curve (AUC). TUG (AUC=0.769, 95% confidence interval: 0.60-0.938, p=0.013). 10MWT (AUC=0.707, 95% confidence interval: 0.523-0.890, NS at p=0.056).

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PAPER 31

Oncologic and functional outcomes of iliosacral resection without reconstruction for primary bone tumours

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Background: A type I pelvic resection for tumour creates a large segmental pelvic ring defect, the management of which remains controversial as the surgeon may or may not reconstruct the resultant pelvic defect. When no reconstruction is performed, the residual ilium collapses back onto the remaining sacrum over time thereby creating an iliosacral pseudarthrosis.

Purpose: The goal of this study was to evaluate the oncologic outcome, complications and functional outcomes of type 1 pelvic resections without reconstruction compared to those who underwent reconstruction.

Patients and Methods: Thirty-seven patients who required a type 1 pelvic resection for tumour with resultant pelvic ring discontinuity between 1989 and 2015 were retrospectively reviewed from our maintained database. Local recurrence-free, disease-free and overall survival were assessed using the Kaplan-Meier method. Patient function was assessed using the Musculoskeletal Tumor Society (MSTS) scoring system and the Toronto Extremity Salvage Score (TESS).

Results: The 14 women and 23 men had a median age of 32 years (15-85). The diagnoses were 19 chondrosarcoma, 4 osteosarcoma, 4 Ewing's, 5 other bone sarcomas and 5 GCT. At mean follow-up of 83 months (1-217), 30 patients were alive without disease, 5 were dead of disease and 2 were deceased of other causes. 4 patients presented with metastatic disease; there were no local recurrences and 5 patients developed subsequent metastatic disease. 5-year local recurrence free survival was 100%, 5-year metastasis-free survival was 83.8% and overall survival was 80.2%. Only 4/37 (11%) patients had a reconstruction of the defect. 20 patients (54%) experienced at least 1 complication, including all 4 reconstructions: 15 wound healing complications/ infections, 3 fractures, 1 pulmonary embolism and 1 retained broken drain. Most complications were early; 4 patients had multiple complications. The mean score for MSTS 87 was 21.1 (+/- 7.8), MSTS 93 was 65.9 (+/-23.8) and TESS was 76.4 (+/-19.3).

Conclusion: Patients requiring type 1 pelvic resections had a very good oncologic outcome. Complication rates were reasonable and generally acute in nature. These resections result in good functional outcomes without reconstruction of the defect.

PAPER 32

Results of PROMIS Physical Functional and Pain Interference Scores in Surgically Treated Patients with Metastatic Bone Disease: Analysis after Early Patient Enrollment in a Multicenter, Prospective Study.

Authors: Alan T Blank MD, MS; Daniel M Lerman MD; Sara Shah BS; Yue Zhang PHD; Wei Liu MPH; Man Hung PHD;Kevin B. Jones, MD; R. Lor Randall MD, FACS

Background: Approximately 20% of cancer related US health care dollars (12 billion $) are spent managing skeletal related events. Furthermore, the prevalence of metastatic bone disease (MBD) grows each year as patients continue to live longer with their disease. Currently in the US, more than 250,000 patients have MBD. MBD is quite painful, debilitating and is also associated with increased morbidity and mortality. Much has been published regarding the benefits of surgical treatment of metastatic bone disease including improved function, decreased in hospital morbidity, and significant cost savings. Evaluating changes in functional and pain levels before surgery to after can be difficult. *Patient Reported Outcomes Measurement Information System* (PROMIS) is a simple, validated computerized adaptive questionnaire, which collects information about patient physical, mental and social health. This test often takes no longer than a few minutes to complete and can consist of as little as five questions. Due to the test's validity as well as ease of use, this is an ideal tool to evaluate patient reported outcomes in pain and function for patients treated surgically for MBD.

Questions/Purpose: Using PROMIS instruments, do patients' physical function and pain assessment scores improve after surgical treatment for metastatic bone disease?

Patient and Methods: This is an IRB approved, multicenter, prospective study involving patients treated surgically for MBD. All patients must have been treated surgically for a metastatic bone lesion. Patients were enrolled preoperatively and contacted by a research coordinator or surgeon from each clinical site postoperatively at routine intervals in order to complete the questionnaires. Basic demographic and disease related data were recorded as well as the PROMIS instruments for Pain Interference and Physical Function. Descriptive analysis of all data was performed. PROMIS scores were collected longitudinally and summarized at each point of time to evaluate average change in score over period of time. Statistical software used was SAS 9.4(SAS Institute Inc., Cary NC).

Results: A total of 43 records of 13 patients at 9 possible periods of time were recorded: baseline, 1 week, 2 weeks, 4 weeks, 6 weeks, 10 weeks, 3 months, 5 months, 6 months. Eight patients were female; 12 patients were Caucasian. Regarding site of surgery, 1 (7.7%) patient had impending acetabular fracture; 8 (61.5%) patients had impending femur fracture; 1 (7.7%)

patient had impending femur and acetabular fracture; 2 (15.4%) patients had realized acetabular fracture and impending femur fracture. Regarding preoperative pain, 1 (7.7%) patient had mild pain; 5 (38.5%) patients had functional pain; 6 (46.2%) patients had severe even at rest pain. Patients' primary type of malignancy was breast (39%), melanoma (8%), myeloma (23%), prostate (23%) and urachal (7%). Thirty-eight percent of patients had radiation treatment prior to surgery. Seven (53.8%) patients had an intramedullary nail; 1 (7.7%) patient had Plate/screw construct, 4 (30.8%) patients had an arthroplasty. Regarding change in physical function score from baseline, the average change at week 1 was -2.5 (SD=5.4), at 2 weeks 1.7 (SD=7.6), after 4 weeks 6.9 (SD=10), after 6 weeks 6.4 (SD =10.9), after 10 weeks 15.3 (SD=3.1), and after 3 months 8.6 (SD=7.6). Regarding change in pain inference score from baseline, the average change at week 1 was -1.2 (SD=7.3), at 2 weeks -2.1 (SD=9.5), after 4 weeks -12.6 (SD=4.5), after 6 weeks -8.3 (SD =10.2), after 10 weeks -16.6 (SD=4.3), and after 3 months -11.4 (SD=8.2).

Conclusion: MBD becomes more prevalent each year and can be painful and functionally debilitating. PROMIS provides an efficient and effective means of determining how patients' physical functional levels of pain change during the pre and postoperative period of surgery for their boney disease. This study provides proof of concept that collecting PROMIS data on patients with metastatic bone disease is not only feasible but also more easily obtained than other more cumbersome means. Due to the cohort size during early patient enrollment we were unable to reach any levels of statistical significance with our PROMIS data. We did see trends of both increasing physical function and decreasing levels of pain interference after surgery for metastatic bone disease. Continuing our multicenter, prospective enrollment will hopefully elucidate more useful information regarding pain and function in surgically treated patients with metastatic bone disease.

PAPER 33

8th Edition AJCC Staging Manual Updates: Mini Symposia Changes to AJCC Bone and Soft Tissue Sarcoma Staging."

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This mini- symposium session will present to the MSTS membership the new changes to bone and soft tissue sarcoma staging, with specific attention to case examples, panel discussion by MSTS members who served on the editorial board of the AJCC, and Q and A. The importance of AJCC cancer staging accuracy is heightened by the mandatory requirement that Commission on Cancer-accredited hospitals use the AJCC TNM system for cancer reporting, which prompted the education of all physicians and registrars in its use.

Prior versions of the AJCC Staging manual have not separated soft tissue sarcomas by anatomic site, and have been limited in ability to discriminate by size. The 8th edition of the AJCC manual has made several important changes reflecting these factors.

Prior versions of the AJCC Staging manual have not separated axial bone sarcomas from appendicular bone sarcomas as separate anatomic site groups for purposes of reporting. As the clinical outcomes of spine and pelvic bone sarcomas are known to be inferior to those that occur in the appendicular skeleton, the 8th edition of the AJCC Staging manual now reflects separate site groups for the spine and pelvis, in addition to the appendicular skeleton.

The Eighth Edition of the *AJCC Cancer Staging Manual*, published in October 2016, goes live in Jan 2018. This is a compendium of all currently available information on the staging of adult cancers for all clinically important anatomic sites. It builds on a rich historical legacy of dynamic vision, international synergy, and the robust principles of cancer classification using the anatomic extent of disease tumor, lymph node, metastasis (TNM) concept. In contrast to prior editions, a much larger editorial board with an editor-in-chief and wide representation of multidisciplinary groups of specialists, from surgical oncology, radiation oncology, medical oncology, anatomic and molecular pathology, imaging, biostatistics, population sciences, the registrar community, and key administrative staff, was created. Seven AJCC Cores, with defined functions and expertise, were introduced: Precision Medicine Core, Evidence Based Medicine and Statistics Core, Imaging Core, Content Harmonization Core, Data Collection Core, Professional Organization and Corporate Relationship Core, and Administrative Core. Disease sites, each typically containing several anatomically related cancers, were reorganized into 18 expert panels. In all, approximately 420 contributors from 181 institutions, 22 countries, and 6 continents participated in the massive and coordinated effort to produce the Eighth Edition.

The tables and images provided are visual aids reproduced from the new Bone and Soft Tissue Sarcoma chapters, 8th edition of the American Joint Commission on Cancer (AJCC) Staging Manual, with permission. For more information regarding the 8th edition please see:

1) The latest information regarding the AJCC 8th Edition Cancer Staging Compton System can be found at **www.cancerstaging.org**

2) The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging
Mahul B. Amin, Frederick L. Greene, Stephen B. Edge, Carolyn C. Compton, Jeffrey E. Gershenwald, Robert K. Brookland, Laura Meyer, Donna M. Gress, David R. Byrd and David P. Winchester
Version of Record online: 17 JAN 2017 | DOI: 10.3322/caac.21388

3) In order to ensure that the cancer care community has the necessary infrastructure in place for documenting 8th Edition stage, the AJCC Executive Committee, in dialogue with the National Cancer Institute (NCI-SEER), Centers for Disease Control and Prevention (CDC), the College of American Pathologists (CAP), the National Comprehensive Cancer Network (NCCN, the National Cancer Data Base (NCDB), and the Commission on Cancer (CoC), made the decision to delay the implementation of the 8th Edition Cancer Staging System to January 1, 2018. Clinicians will continue to use the latest information for patient care, including scientific content of the 8th Edition Manual. All newly diagnosed cases through December 31st 2017 should be staged with the 7th edition.

Soft Tissue Sarcoma

Summary of Changes

Change	Details of Change	Level of Evidence
New chapter	Soft tissue sarcoma was divided into chapters by anatomic site.	N/A
Definition of Primary Tumor (T)	Superficial and deep location has been removed as part of T criteria.	II
Definition of Primary Tumor (T)	T categories have been increased from two to four.	II
Definition of Primary Tumor (T)	T1 remains as tumor 5 cm or less in greatest dimension.	II
Definition of Primary Tumor (T)	T2 is now tumor more than 5 cm and less than or equal to 10 cm in greatest dimension.	II
Definition of Primary Tumor (T)	T3 is newly categorized as tumor more than 10 cm and less than or equal to 15 cm in greatest dimension.	II[1]
Definition of Primary Tumor (T)	T4 is a new category defined as tumor more than 15 cm in greatest dimension	II[1]
AJCC Prognostic Stage Groups	AJCC Prognostic Stage Groups have been changed.	II

M.B. Amin et al. (eds.), *AJCC Cancer Staging Manual, Eighth Edition*, DOI 10.1007/978-3-319-40618-3_39

Soft Tissue Sarcoma

Definition of Primary Tumor (T)

T Category	T Criteria
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor 5 cm or less in greatest dimension
T2	Tumor more than 5 cm and less than or equal to 10 cm in greatest dimension
T3	Tumor more than 10 cm and less than or equal to 15 cm in greatest dimension
T4	Tumor more than 15 cm in greatest dimension

Definition of Regional Lymph Node (N)

N Category	N Criteria
N0	No regional lymph node metastasis or unknown lymph node status
N1	Regional lymph node metastasis

Definition of Distant Metastasis (M)

M Category	M Criteria
M0	No distant metastasis
M1	Distant metastasis

Definition of Grade (G)

FNCLCC Histologic Grade – see Histologic Grade (G)

G	G Definition
GX	Grade cannot be assessed
G1	Total differentiation, mitotic count and necrosis score of 2 or 3
G2	Total differentiation, mitotic count and necrosis score of 4 or 5
G3	Total differentiation, mitotic count and necrosis score of 6, 7, or 8

AJCC PROGNOSTIC STAGE GROUPS

When T is…	And N is…	And M is…	And grade is…	Then the stage group is…
T1	N0	M0	G1, GX	IA
T2, T3, T4	N0	M0	G1, GX	IB
T1	N0	M0	G2, G3	II
T2	N0	M0	G2, G3	IIIA
T3, T4	N0	M0	G2, G3	IIIB
Any T	N1	M0	Any G	IV
Any T	Any N	M1	Any G	IV

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Bone Sarcoma

Summary of Changes

Change	Details of Change	Level of Evidence
Definitions of AJCC TNM	Pelvis and spine each have a separate and distinct TNM classification but not a separate stage grouping.	III
AJCC Prognostic Stage Groups	Stage III is reserved for G2 and G3.	III
Histologic Grade (G)	G4 designation has been eliminated (G1, low grade; G2 and G3, high grade).	III

Definition of Primary Tumor (T)

Appendicular Skeleton, Trunk, Skull, and Facial Bones

T Category	*T Criteria*
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor ≤8 cm in greatest dimension
T2	Tumor >8 cm in greatest dimension
T3	Discontinuous tumors in the primary bone site

Spine

T Category	*T Criteria*
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor confined to one vertebral segment or two adjacent vertebral segments
T2	Tumor confined to three adjacent vertebral segments
T3	Tumor confined to four or more adjacent vertebral segments, or any nonadjacent vertebral segments
T4	Extension into the spinal canal or great vessels
T4a	Extension into the spinal canal
T4b	Evidence of gross vascular invasion or tumor thrombus in the great vessels

Pelvis

T Category	*T Criteria*
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor confined to one pelvic segment with no extraosseous extension
T1a	Tumor ≤8 cm in greatest dimension
T1b	Tumor >8 cm in greatest dimension
T2	Tumor confined to one pelvic segment with extraosseous extension or two segments without extraosseous extension
T2a	Tumor ≤8 cm in greatest dimension
T2b	Tumor >8 cm in greatest dimension
T3	Tumor spanning two pelvic segments with extraosseous extension
T3a	Tumor ≤8 cm in greatest dimension
T3b	Tumor >8 cm in greatest dimension
T4	Tumor spanning three pelvic segments or crossing the sacroiliac joint
T4a	Tumor extent medial to the sacral neuroforamen
T4b	Tumor encasement of external iliac vessels or presence of gross tumor thrombus in major pelvic vessels

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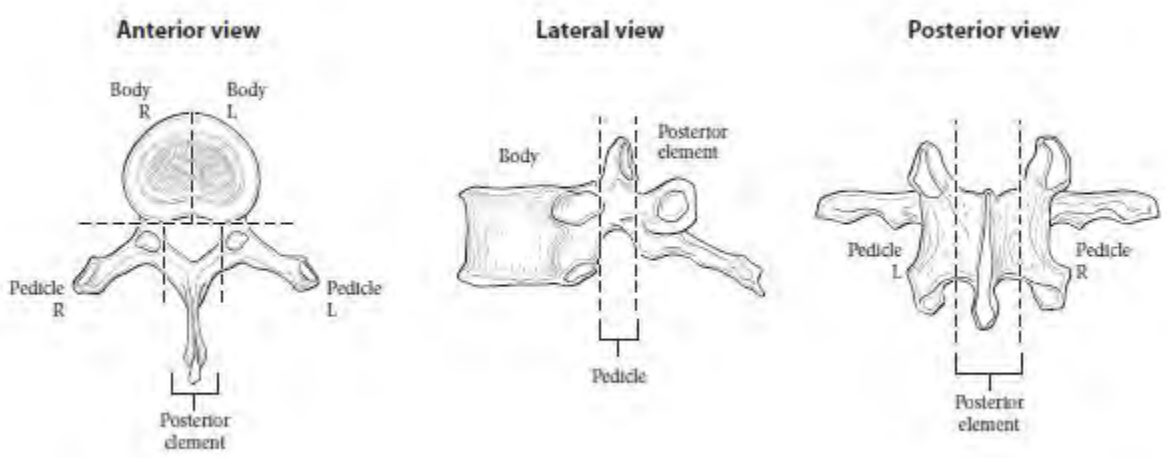
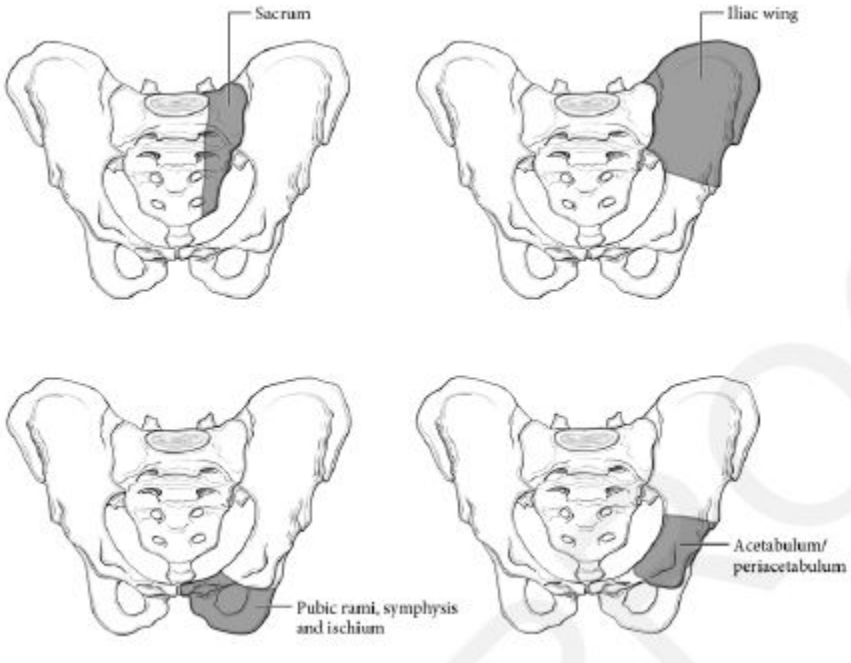
Spine Segments for Staging



Pelvic Segments for Staging



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PAPER 34

Stability and Instability in Ewing Sarcoma: The Relationship Between DNA Repair and p53

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Background: An EWS-ETS family translocation is necessary but not sufficient for Ewing sarcoma (ES) generation, with the remaining components for tumorigenesis and metastasis remaining largely unknown and highly variable[1]. To better understand these unknown factors and their contribution to clinical prognosis, recent efforts have focused on the genomic characterization of ES. Some investigators have studied gene mutations and others have explored copy number alterations (CNAs) and epigenetics. While ES overall has a low mutation rate compared to other tumors, somatic mutations in three genes are common: *STAG2*, *CDKN2A*, and *TP53*[2, 3]. *STAG2* and *CDKN2A* both correlate with *TP53* in that co-mutation of *STAG2* and *TP53* shows a synergistic effect to increase genetic instability[3], and wild-type *CDKN2A* has a stabilizing effect on *TP53*. Further, multiple studies have shown a correlation with increased CNA and worse survival and others have correlated a methylation anomaly with altered expression of *CDKN2A*[4].

While the correlation of *TP53* status with CNAs and resultant phenotypic change in ES has been established, the potential role of DNA repair mechanisms in this process remains unclear. Recent evidence suggests that ES may be deficient in repairing DNA double stranded breaks (DSBs) following irradiation[5], however, few groups have investigated in depth the role of *TP53* in this process. We hypothesize that defective DNA repair in ES is a function of p53 status.

Questions/Purposes:

1. Determine efficiency of DNA repair of multiple ES cell lines in comparison to other cancers.
2. Determine if transducing a p53-deficient ES cell line with functional *TP53* can improve DNA repair capability.

Methods: Seven ES cell lines (CHLA9, CHLA10, A673, ES-1, ES-8, CHLA258, TC252), two osteosarcoma (OS) cell lines (USOS, SAOS-2) and one ovarian adenocarcinoma cell line (SKOV-3) were cultured and seeded on coverslips. For each cell line, designated coverslips were set aside to mark the zero time point, prior to irradiation. The remaining coverslips were

irradiated at 5Gy and grouped according to four additional time points post irradiation: 5 minutes, 2 hours, 8 hours, and 24 hours. All coverslips were then immunostained for γ-H2AX and mounted on slides to indirectly measure DSBs in the DNA. For each slide, fifty cells were imaged and γ-H2AX foci were counted objectively by converting the images to binary with ImageJ. Following this, A673 cells, which harbor a known p53 mutation, were transduced with a lentivirus vector system with either an empty vector or the TP53 gene. The above immunofluorescence experiment was then repeated.

Results: The visual DNA repair response following irradiation confirmed dramatic increase in γ-H2AX foci, and thus DSBs in cells following irradiation at 5Gy. CHLA9 (with wild-type p53) returns to near normal baseline DNA damage 24 hours post irradiation, as illustrated by percentage of cells with > 20 γ-H2AX foci at each time point (Fig. 1). CHLA10 (recurrent ES in same patient as CHLA9, with mutated p53) continues to have significant DNA damage above baseline after 24 hours (Fig. 1). Of all cell lines tested, those with p53 alterations consistently show more DNA damage above baseline 24 hours post irradiation than those with wild type (WT) p53 (Fig. 2A). Further, A673 cells that have been transduced to express WT p53 show a marked reduction in DNA damage than those transduced with an empty vector (Fig. 2A and 2B).

Conclusions: Deficient DNA repair in certain ES cell lines has a positive correlation with *TP53* mutations. By transducing p53-defective ES cell lines with WT p53, the DNA repair mechanism can be partially restored. Further work is necessary to determine ES development mechanisms beyond EWS-ETS family translocations, but our evidence suggests that p53 mutations leading to defective DNA repair may play a pivotal role in tumorigenesis and clinical progression in a subset of ES patients.

Figures:

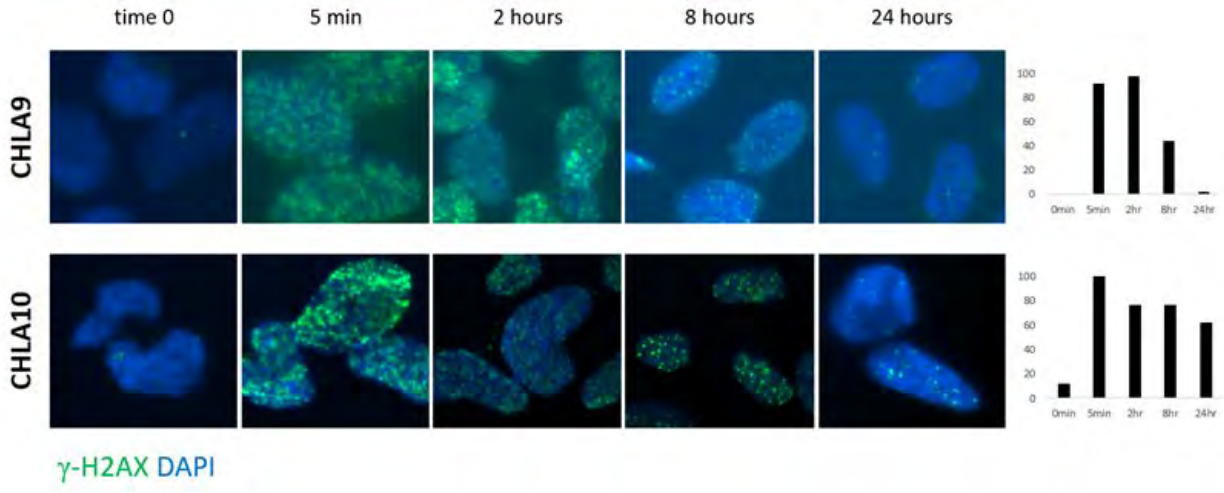

Figure 1: Representative micrographs of CHLA9 and CHLA10 nuclei prior to irradiation at 5Gy as well as 5 minutes, 2 hours, 8 hours, and 24 hours after

irradiation. Nuclei are stained blue and γH2AX nuclei are stained green. Histograms represent proportion of cells with > 20 foci of γH2AX per cell.

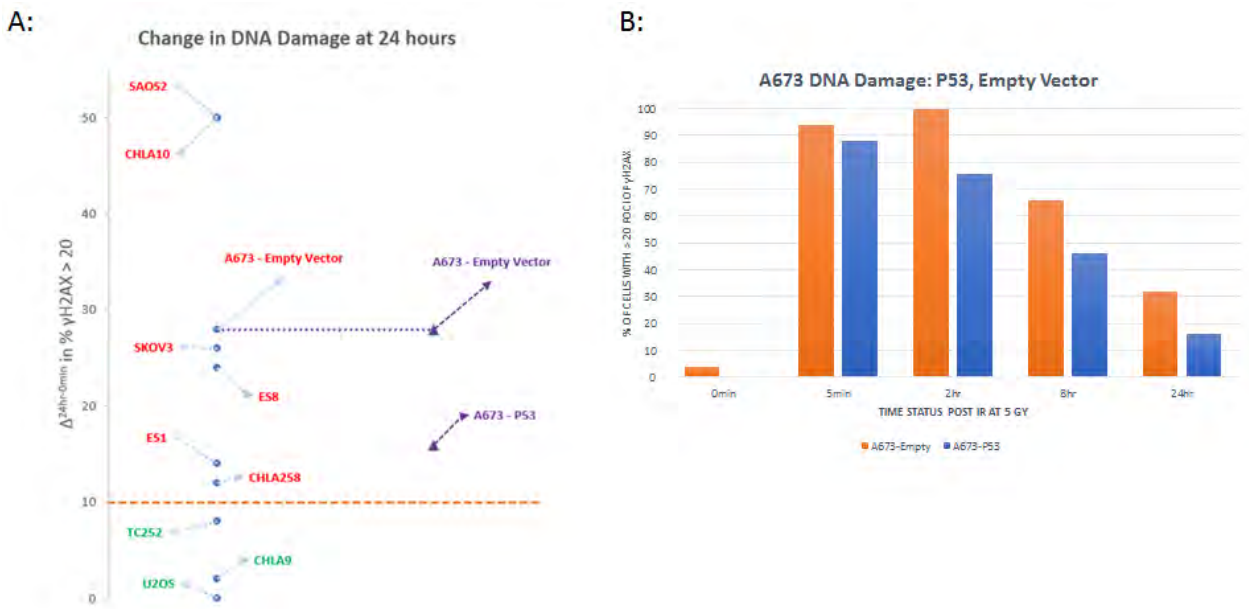

Figure 2. (A) For all cell lines tested, the proportion of cells with >20 foci of γH2AX 24 hours after IR at 5Gy were compared to those that did not receive IR. Cell lines labeled in red have known alterations of p53. Cell lines labeled in green have known wild type p53. The A673 cell line was transduced with wild type p53 and showed an increase in DNA repair 24 hours after IR (purple). (B) Histogram comparing A673 cells transduced with an empty vector (orange) to those transduced with TP53 (blue).

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PAPER 35

Oxygen sensing by T cells establishes the lung as an immunologically favorable metastatic niche

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Background: Metastasis is responsible for greater than 90% of all cancer deaths and remains a paramount clinical and scientific challenge to physicians and patients[1]. For osteosarcoma the 5-year survival rate for localized disease is 60-80%, however this rate drops to approximately 15% when the cancer has metastasized[2]. The lung is the most common site for metastasis in many cancer histologies including osteosarcoma. Moreover, cancers are frequently lethal when they have spread to the lungs. The "seed and soil" hypothesis of metastasis postulates that properties of both the cancer cell (seed) as well as the site of metastasis (soil) are important in permitting the formation of metastases. An emerging concept in metastatic biology is the notion that cancer cells must evade immune responses at distant sites in order to establish metastases[3]. In line with the seed and soil hypothesis, we hypothesized that lung-specific immunoregulatory mechanisms create an immunologically permissive environment for cancer metastasis. T cells, a specialized type of immune cell, are critical in establishing pulmonary immunologic tolerance. The mechanisms that govern T cell function in the lung, and how these contribute to cancer metastasis remains to be elucidated. We considered that molecular oxygen, which is present in high concentrations in the lung, might influence T cell behavior and permit pulmonary metastasis.

Purpose: We thus sought to investigate site-specific pulmonary immunoregulatory mechanisms in an effort to elucidate how metastatic tumor cells evade immune mediated destruction upon colonization of the lung. Specifically, we aimed to determine whether oxygen influences T cell

behavior to support pulmonary tolerance. We also sought to determine whether oxygen plays a role in establishing the lung as a favorable metastatic site. Finally, we aimed to inhibit the immunosuppressive effects of molecular oxygen in order to promote anti-tumor immunity and limit cancer metastasis to the lung.

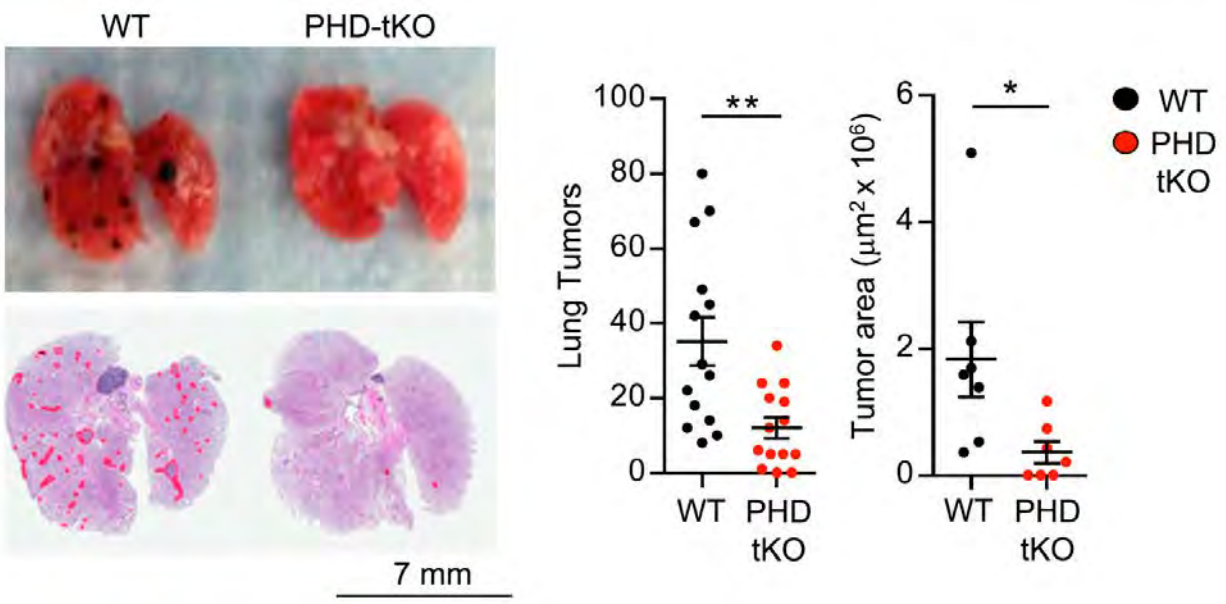
Methods: Cells sense environmental oxygen through a family of three proteins called the prolyl-hydroxylase domain (PHD) proteins. We generated a knock-out mouse model in which all three PHD proteins are selectively deleted from T cells using the *CD4*-Cre transgenic system (PHD-tKO). This allowed us to selectively explore the role that molecular oxygen plays in influencing T cell behavior and how this contributes to establishing an immunologically tolerant environment for cancer metastasis to the lung. To this end, we employed experimental models of cancer metastasis and adoptive T cell transfer immunotherapy in PHD-tKO mice and littermate matched wild-type controls.

Results: We found that T-cell-intrinsic expression of the oxygen-sensing prolyl-hydroxylase (PHD) proteins is required to maintain local tolerance against innocuous antigens in the lung but powerfully licenses colonization by circulating tumor cells. PHD proteins limited inflammatory pulmonary type helper (Th)-1 responses, promoted immunosuppressive CD4(+)-regulatory T (Treg) cell induction, and restrained CD8(+) T cell effector function. Tumor metastasis to the lung was accompanied by PHD-protein-dependent induction of pulmonary Treg cells and suppression of IFN-γ-dependent tumor clearance. Most important to potential therapeutic translation, we found that T-cell-intrinsic deletion or pharmacological inhibition of PHD proteins limits tumor colonization of the lung and improves the efficacy of adoptive cell transfer immunotherapy **(Figure 1)**. These findings have recently been published[4].

More recently, we have revealed that protection from lung metastasis in PHD-tKO mice requires an influx of inflammatory T cells that is suppressed by oxygen sensing. Additionally, provision of wild type Treg cells was sufficient to permit lung metastasis in PHD-tKO mice. Finally, we have extended our findings in lung metastasis to reveal that oxygen mediated T cell suppression is also important in creating hospitable metastatic environments in other well vascularized sites including the liver.

Conclusion: Collectively, the oxygen-sensing PHD proteins function in T cells to coordinate distinct immunoregulatory programs within the lung and other well-vascularized tissues that are permissive to cancer metastasis. This work identifies a novel mechanism by which an environmental factor, molecular oxygen, influences T cell differentiation and function in order to establish pulmonary tolerance in the healthy state. Consequently, the immunoregulatory effect of oxygen supports cancer metastasis to the lung. Importantly, our studies identify a new therapeutic strategy to restore immune reactivity against metastatic cancer.

Figure 1. Oxygen-sensing PHD proteins in T cells permit cancer metastasis to the lung.



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PAPER 36

Osteoblast inhibition is a Novel Mechanism For Development of Osteolytic Lesions in Renal Cell Bone Metastasis

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Background: The development of metastasis in bone is common in renal cell cancer (RCC) progression. RCC bone metastases are characteristically osteolytic. The mechanism of bone destruction in RCC bone metastasis is unknown. In

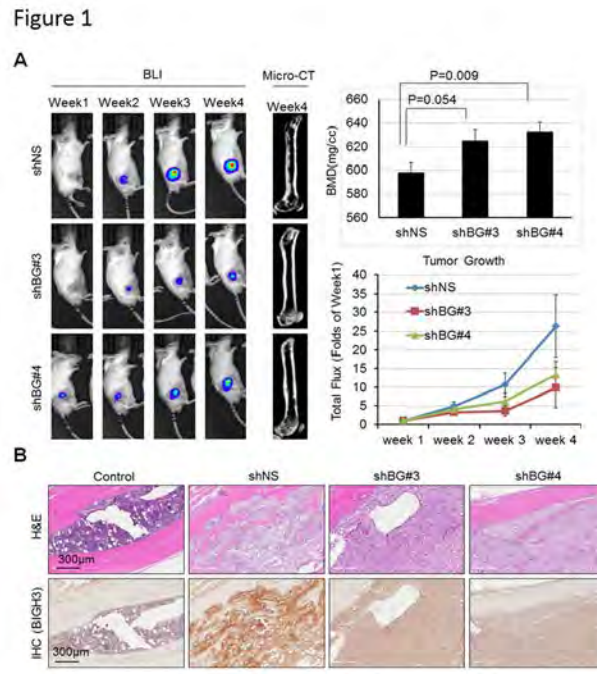

Fig 1. BIGH3 knockdown alleviates osteolytic lesions in mouse xenograft model for RCC bone metastasis. A. BIGH3 knoeckdown cell lines #3 and #4 were injected into the femur of mouse right legs for 4 weeks. 786-shNS cells were used as control. BLI, microCT, and quantification of BMD are shown. B. H&E stained bone section of an injected femur showed the presence of tumor cells and immunohistochemistry of BIGH3 on the adjacent sections of H&E for knockdown cells lines (#3 and #4) and non-silencing controls (786-shNS).

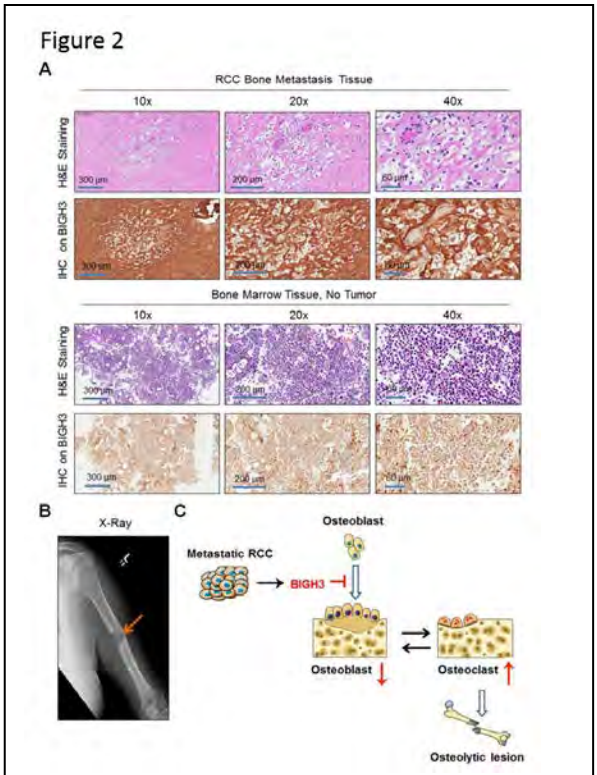

Fig. 2 BIGH3 expression is maintained in human RCC bone metastasis. A. BIGH3 expression determined by immunohistochemistry staining in bone metastasis and normal bone marrow at 10X,20X and 40X. B. Xray showing the source of bone metastasis material from pathologic humerus fracture site. C. Proposed role of BIGH3 in tipping bone homeostatsis towards osteolysis.

this study, we showed that suppression of osteoblast differentiation is one of the mechanisms that enhance the osteolytic progression of RCC in bone. After forming, there is a high incidence of pathologic fractures and subsequent disease progression. Understanding the molecular mechanisms involved will identify strategies for treating bone metastases more efficaciously. Tumor cells from RCC have previously been thought to constitutively activate osteoclasts. However, evidence for RANKL expression in RCC *bone metastases* has been difficult to demonstrate either in patients or *in vitro*. Moreover, the frequently observed resistance to treatments based solely on inhibiting RANKL mediated osteolysis indicates that additional mechanisms are at work. A pathological osteolytic phenotype can also be produced by the concomitant reduction in bone formation, leading to a relative increase in bone destruction from osteoclasts. Whether such a mechanism is involved in RCC bone metastasis has not been examined. Our studies have shown that an osteolytic metastatic clear cell RCC cell line, 786-O Bo, secretes BIGH3, a TGF inducible protein that inhibits osteoblast differentiation, potentially contributing to osteolysis in RCC bone metastasis. (**Figure 2C**).

Questions/Purposes:

1. Determine whether a mechanism of BIGH3 mediated osteoblast suppression is involved in RCC bone metastasis formation.
2. Determine whether BIGH3 is present at osteolytic bone metastasis sites in RCC patients.

Methods: In order to study the possibility of osteoblast inhibition, we used a SCID mouse xenograft for osteolytic bone metastasis. We used a clear cell RCC cell line, 786-O Bo that homes to bone and creates osteolytic metastasis. BIGH3 was then knocked down in 786-O Bo cell lines using shRNA. These cells were then evaluated for ability to form osteolytic metastases via injection in SCID mice femora. Human bone metastasis samples were collected and evaluated for BIGH3 expression via immunohistochemical staining.

Results: Knockdown of BIGH3 in Bo-786 cells reversed the inhibition of osteoblast differentiation. Injection of 786/shBIGH3 cells into mouse femurs reduced osteolytic bone lesions compared with the parental 786-O cells. (**Figure 2**) In bone metastasis specimens from patients with metastatic RCC, immunostaining showed that all 18 specimens expressed BIGH3, with 11 stained strong positive and 7 weak positive.

Conclusions: BIGH3 inhibits osteoblast differentiation and bone formation in RCC bone metastasis. BIGH3 inhibition via knockdown reduces osteolytic bone metastasis formation in SCID mice. Taken together, this evidence supports an alternative possibility that centers on osteoblast inhibition (rather than osteoclast activation) for producing osteolytic bone metastases in renal cell carcinoma. Whether these factors affect osteoclasts, osteocytes, or have an autocrine effect on metastatic cells, is unknown and will be the focus of future work.

PAPER 37

Precision Medicine for the Treatment of Osteosarcoma: ATRX Deficiency Predicts Enhanced Sensitivity to rTRAIL

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Background: Osteosarcoma is the most common primary bone tumor, and the second most common malignancy in adolescents.[1] Although the overall survival of osteosarcoma patients was significantly improved by the addition of chemotherapy in the 1980s, there have been few advances in systemic therapy and survival outcomes since that time, with current 10-year survival rates of only 20-30% in patients with detectable metastatic disease on presentation. Current systemic therapies have narrow toxicity profiles and variable response rates with up to 50% of patients deemed "poor responders" to traditional chemotherapy agents. Thus, finding new, targeted therapies for osteosarcoma is imperative. A major barrier to identifying new therapies has been the limited access to patient samples and model systems to study this rare disease. To overcome this barrier, we have turned to pet dogs with spontaneously occurring osteosarcoma. Although osteosarcoma is uncommon in humans, it is relatively common in dogs. In addition, gene expression in human and dog osteosarcomas are indistinguishable from one another[2]. With these similarities in mind, we mined human and dog osteosarcoma data to identify mutations that may predict susceptibility to new treatments. This comparative oncology approach has recently identified ATRX (α thalassemia /mental retardation X-linked) as one of a small number of genes commonly mutated in osteosarcomas of both dogs and humans.[3,4] Recent studies using genome sequencing have demonstrated mutations of ATRX in up to 30% of human osteosarcomas.[5-7] Given that ATRX mutation is highly associated with osteosarcoma across species, we believe it plays an important role in the pathogenesis of disease, and can be leveraged to identify new, targeted therapies.

Questions/Purposes:

1. To describe our cross-species platform for drug discovery, facilitating a precision approach to the treatment of osteosarcoma.
2. To screen and validate candidate drugs to which loss of ATRX may confer sensitivity.

Methods: The bio-informatics database, "Genomics of Drug Sensitivity in Cancer" correlates genetic and molecular features of cancers with response to anti-cancer drugs. We performed an analysis, including all cancer types, of various drug effects stratified by ATRX mutation status. We then attempted to validate increased sensitivity in ATRX deficient osteosarcoma cells, with each drug identified in this screen. We used RNA interference to knock down ATRX mRNA and protein in human osteosarcoma cell lines and tested the sensitivity to candidate drugs with and without ATRX knockdown. We used western blotting to confirm knockdown of ATRX in the osteosarcoma cells. Cells were incubated with candidate drugs for 48h, and cell viability was compared to vehicle-treated control wells using CellTiter-Glo assays.

Results: The bioinformatics screen identified four drugs with apparent increased effectiveness in ATRX-deficient cell populations. These drugs included: ZM-447439 (Aurora kinase B inhibitor), Avagacestat (γ-secretase inhibitor), human recombinant TRAIL (Death Receptor 4/5 agonist), and Linifanib (VEGF/PDGF antagonist). Of these four drugs, human recombinant TRAIL (rTRAIL) showed a consistently significant decrease in cell viability in the ATRX knockdown conditions as compared to the non-silencing controls (in which ATRX was present) in both 143B ($p<0.01$) and MG-63 ($p<0.001$) osteosarcoma cell lines (Figures 1 and 2).

Conclusions: In this study, we demonstrate that deficiency in ATRX conferred increased sensitivity to the pro-apoptotic drug, rTRAIL. TRAIL (TNF-related apoptosis-inducing ligand) is a member of the TNF superfamily of cytokines that function to activate the external apoptosis pathway via binding and crosslinking of death receptors. Previous studies have demonstrated increased expression of death receptors in various malignancies,[8,9] as well as the ability of rTRAIL to induce apoptosis selectively in a wide variety of tumor cells, while sparing vital normal cells.[10,11] Unlike many existing chemotherapeutic agents, the high specificity and minimal systemic toxicity of rTRAIL are highly coveted properties of a potential anti-cancer drug. Our work describes a novel approach to drug discovery, with the goal of identifying targeted therapies that can be used in a precision model of treatment for osteosarcoma. Furthermore, these findings provide a framework for clinical development of rTRAIL in the osteosarcoma patient subset for which ATRX is lost.

Figures:

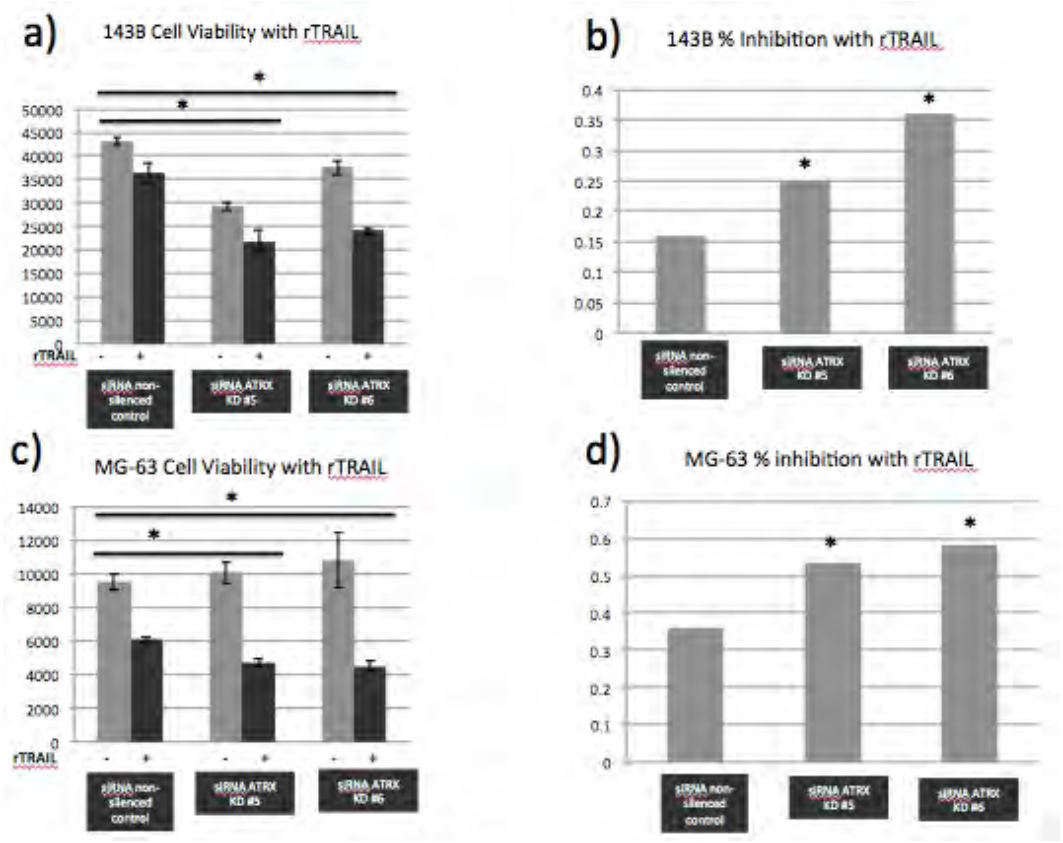
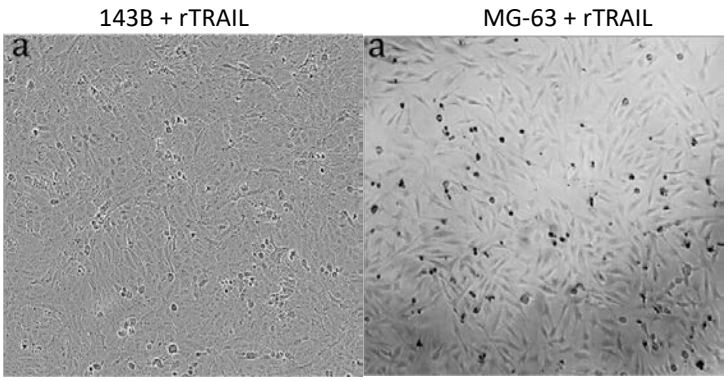


Figure 1: Cell viability of human osteosarcoma cell lines after treatment with human recombinant TRAIL (rTRAIL) in two independent ATRX knockdown conditions (right two columns) compared to non-silencing control (left). rTRAIL was added and compared to each cell condition against PBS control. Cell viability (a,c), also expressed as % inhibition (b.d), was assessed using the CellTiter-Glo assay. Significantly greater cell inhibition (noted by asterisk) is seen with treatment in the ATRX deficient cell populations compared to the non-silencing control.



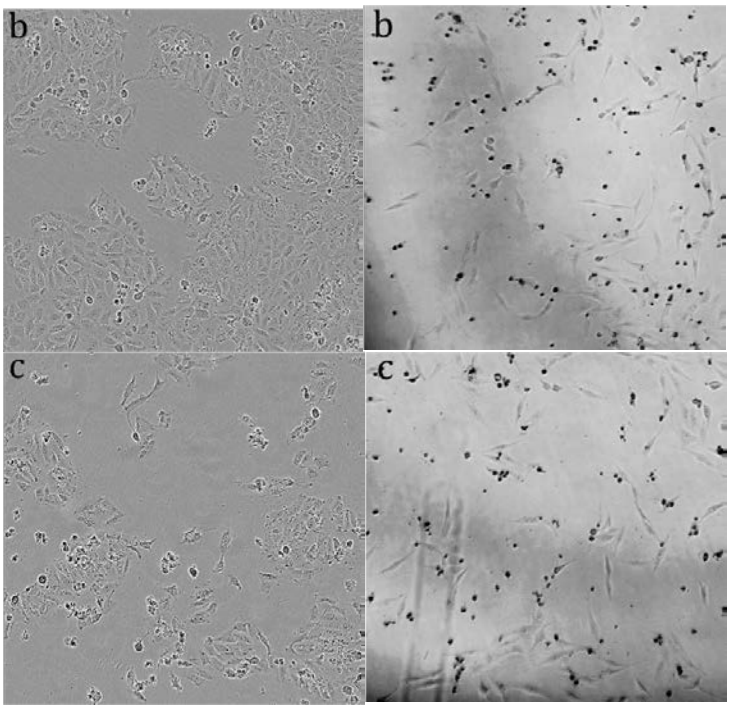


Figure 2: Microscopic images of osteosarcoma cells treated with rTRAIL after 48hrs. (a) siRNA non-silencing control, (b) siRNA ATRX #5 knockdown, (c) siRNA ATRX #6 knockdown

References:

1. Arndt CA, Crist WM. Common musculoskeletal tumors of childhood and adolescence. The New England journal of medicine 1999;341:342-52.
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10. de Miguel D, Lemke J, Anel A, Walczak H, Martinez-Lostao L. Onto better TRAILs for cancer treatment. Cell death and differentiation 2016;23:733-47.
11. Walczak H, Miller RE, Ariail K, et al. Tumoricidal activity of tumor necrosis factor-related apoptosis-inducing ligand in vivo. Nature medicine 1999;5:157-63.

PAPER 38

The Most Cited Articles In Orthopaedic Oncology

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Background: Rank lists of the most cited articles serve to identify important studies that have influenced practice, generated discussion, and advanced the sciences of their respective fields.

Purpose: The purpose of this study was to analyze the characteristics of the 50 most cited articles overall and by decade in orthopaedic oncology.

Methods: We searched the Science Citation Index Expanded database and analyzed each article for the following characteristics: topic, type of article (basic science vs. clinical research), authorship, institution and country of first author, journal and year of publication, and level of evidence per *Clinical Orthopaedics and Related Research (CORR)* guidelines.

Results: The overall top 50 articles were published between 1966-2016, cited an average of 282 times, and with 29 (58%) being level IV evidence. Compared over time, level of evidence of the more cited papers improved from 0% level II and 82% level IV from 1966-1979, to 6% level II and 38% level IV from 2010-2016. In addition, the number of articles and average level of evidence contributed by decade to the overall top 50 list improved, 8 (3.875) between 1966-1979, 15 (3.67) between 1981-1989, 18 (3.69) between 1990-1999, and 9 (3.14) between 2000-2009. There was only 1 level I study included in the top 50 list from any decade.

Discussion: This list of the most cited articles in orthopaedic oncology demonstrate an increase in high quality studies published and cited between 1966-2016. Nevertheless, there still is a significant lack of higher level of evidence research (Level I and II) in the area of musculoskeletal oncology. Collaborative studies, a national MSTS registry, international registries, and prospective studies are necessary to improve the quality of published literature in orthopedic oncology.

Table 1. The Top 50 Most Cited Articles in Orthopaedic Oncology

Rank	Article	Number of Citations
1	Enneking WF, Dunham W, Gebhardt MC, Malawar M, Pritchard DJ. A system for the functional evaluation of reconstructive procedures after surgical treatment of tumors of the musculoskeletal system. *Clin. Orthop.* 1993:241–246.	1114
2	Enneking WF, Spanier SS, Goodman MA. A system for the surgical staging of musculoskeletal sarcoma. *Clin. Orthop.* 1980:106–120.	882
3	Goldenberg RR, Campbell CJ, Bonfiglio M. Giant-cell tumor of bone. An analysis of two hundred and eighteen cases. *J. Bone Joint Surg. Am.* 1970;52:619–664.	565
4	Dahlin DC, Coventry MB. Osteogenic sarcoma. A study of six hundred cases. *J. Bone Joint Surg. Am.* 1967;49:101–110.	516
5	Campanacci M, Baldini N, Boriani S, Sudanese A. Giant-cell tumor of bone. *J. Bone Joint Surg. Am.* 1987;69:106–114.	501
6	Barr JD, Barr MS, Lemley TJ, McCann RM. Percutaneous vertebroplasty for pain relief and spinal stabilization. *Spine*. 2000;25:923–928.	455
7	Tomita K, Kawahara N, Kobayashi T, Yoshida A, Murakami H, Akamaru T. Surgical strategy for spinal metastases. *Spine*. 2001;26:298–306.	414
8	Mankin HJ, Lange TA, Spanier SS. The hazards of biopsy in patients with malignant primary bone and soft-tissue tumors. *J. Bone Joint Surg. Am.* 1982;64:1121–1127.	361
9	McKenna RJ, Schwinn CP, Soong KY, Higinbotham NL. Sarcomata of the Osteogenic Series (Osteosarcoma, Fibrosarcoma, Chondrosarcoma, Parosteal Osteogenic Sarcoma, and Sarcomata Arising in Abnormal Bone) AN ANALYSIS OF 552 CASES. *J. Bone Joint Surg. Am.* 1966;48:1–26.	344
10	Mankin HJ, Gebhardt MC, Jennings LC, Springfield DS, Tomford WW. Long-term results of allograft replacement in the management of bone tumors. *Clin. Orthop.* 1996:86–97.	337
11	Enneking WF, Mindell ER. Observations on massive retrieved human allografts. *J. Bone Joint Surg. Am.* 1991;73:1123–1142.	331
12	Marcove RC, Miké V, Hajek JV, Levin AG, Hutter RV. Osteogenic sarcoma under the age of twenty-one. A review of one hundred and forty-five operative cases. *J. Bone Joint Surg. Am.* 1970;52:411–423.	323
13	Mankin HJ, Mankin CJ, Simon MA. The hazards of the biopsy, revisited. Members of the Musculoskeletal Tumor Society. *J. Bone Joint Surg. Am.* 1996;78:656–663.	311
14	Gerszten PC, Burton SA, Ozhasoglu C, Welch WC. Radiosurgery for spinal metastases: clinical experience in 500 cases from a single institution. *Spine*. 2007;32:193–199.	303
15	Rosenthal DI, Hornicek FJ, Wolfe MW, Jennings LC, Gebhardt MC, Mankin HJ. Percutaneous radiofrequency coagulation of osteoid osteoma compared with operative treatment. *J. Bone Joint Surg. Am.* 1998;80:815–821.	297
16	Tokuhashi Y, Matsuzaki H, Oda H, Oshima M, Ryu J. A revised scoring	296

	system for preoperative evaluation of metastatic spine tumor prognosis. *Spine*. 2005;30:2186–2191.	
17	Simon MA, Enneking WF. The management of soft-tissue sarcomas of the extremities. *J. Bone Joint Surg. Am.* 1976;58:317–327.	271
18	Tokuhashi Y, Matsuzaki H, Toriyama S, Kawano H, Ohsaka S. Scoring system for the preoperative evaluation of metastatic spine tumor prognosis. *Spine*. 1990;15:1110–1113.	266
19	Schmale GA, Conrad EU 3rd, Raskind WH. The natural history of hereditary multiple exostoses. *J. Bone Joint Surg. Am.* 1994;76:986–992.	263
20	Enneking WF, Spanier SS, Goodman MA. Current concepts review. The surgical staging of musculoskeletal sarcoma. *J. Bone Joint Surg. Am.* 1980;62:1027–1030.	262
21	Tomita K, Kawahara N, Baba H, Tsuchiya H, Fujita T, Toribatake Y. Total en bloc spondylectomy. A new surgical technique for primary malignant vertebral tumors. *Spine*. 1997;22:324–333.	259
22	Rougraff BT, Simon MA, Kneisl JS, Greenberg DB, Mankin HJ. Limb salvage compared with amputation for osteosarcoma of the distal end of the femur. A long-term oncological, functional, and quality-of-life study. *J. Bone Joint Surg. Am.* 1994;76:649–656.	258
23	Rao AS, Vigorita VJ. Pigmented villonodular synovitis (giant-cell tumor of the tendon sheath and synovial membrane). A review of eighty-one cases. *J. Bone Joint Surg. Am.* 1984;66:76–94.	258
24	Mirels H. Metastatic disease in long bones. A proposed scoring system for diagnosing impending pathologic fractures. *Clin. Orthop.* 1989:256–264.	257
25	Enneking WF, Campanacci DA. Retrieved human allografts : a clinicopathological study. *J. Bone Joint Surg. Am.* 2001;83-A:971–986.	231
26	McDonald DJ, Sim FH, McLeod RA, Dahlin DC. Giant-cell tumor of bone. *J. Bone Joint Surg. Am.* 1986;68:235–242.	231
27	Boriani S, Weinstein JN, Biagini R. Primary bone tumors of the spine. Terminology and surgical staging. *Spine*. 1997;22:1036–1044.	223
28	Parrish FF. Allograft replacement of all or part of the end of a long bone following excision of a tumor. *J. Bone Joint Surg. Am.* 1973;55:1–22.	221
29	Sung HW, Kuo DP, Shu WP, Chai YB, Liu CC, Li SM. Giant-cell tumor of bone: analysis of two hundred and eight cases in Chinese patients. *J. Bone Joint Surg. Am.* 1982;64:755–761.	214
30	Rock MG, Pritchard DJ, Reiman HM, Soule EH, Brewster RC. Extra-abdominal desmoid tumors. *J. Bone Joint Surg. Am.* 1984;66:1369–1374.	207
31	Malawer MM, Chou LB. Prosthetic survival and clinical results with use of large-segment replacements in the treatment of high-grade bone sarcomas. *J. Bone Joint Surg. Am.* 1995;77:1154–1165.	193
32	Lee FY, Mankin HJ, Fondren G, Gebhardt MC, Springfield DS, Rosenberg AE, Jennings LC. Chondrosarcoma of bone: an assessment of outcome. *J. Bone Joint Surg. Am.* 1999;81:326–338.	187
33	O'Donnell RJ, Springfield DS, Motwani HK, Ready JE, Gebhardt MC, Mankin HJ. Recurrence of giant-cell tumors of the long bones after curettage and packing with cement. *J. Bone Joint Surg. Am.* 1994;76:1827–1833.	184
34	Harrington KD. The use of methylmethacrylate for vertebral-body replacement and anterior stabilization of pathological fracture-dislocations of the spine due to metastatic malignant disease. *J. Bone*	180

	Joint Surg. Am. 1981;63:36–46.	
35	Campanacci M, Capanna R, Picci P. Unicameral and aneurysmal bone cysts. *Clin. Orthop.* 1986:25–36.	178
36	Larsson SE, Lorentzon R, Boquist L. Giant-cell tumor of bone. A demographic, clinical, and histopathological study of all cases recorded in the Swedish Cancer Registry for the years 1958 through 1968. *J. Bone Joint Surg. Am.* 1975;57:167–173.	177
37	Boriani S, Bandiera S, Biagini R, Bacchini P, Boriani L, Cappuccio M, Chevalley F, Gasbarrini A, Picci P, Weinstein JN. Chordoma of the mobile spine: fifty years of experience. Spine. 2006;31:493–503.	174
38	Rock MG, Pritchard DJ, Unni KK. Metastases from histologically benign giant-cell tumor of bone. *J. Bone Joint Surg. Am.* 1984;66:269–274.	166
39	Han CS, Wood MB, Bishop AT, Cooney WP 3rd. Vascularized bone transfer. *J. Bone Joint Surg. Am.* 1992;74:1441–1449.	165
40	Harrington KD. Metastatic disease of the spine. *J. Bone Joint Surg. Am.* 1986;68:1110–1115.	162
41	DiCaprio MR, Enneking WF. Fibrous dysplasia. Pathophysiology, evaluation, and treatment. J. Bone Joint Surg. Am. 2005;87:1848–1864.	161
42	Kelly CM, Wilkins RM, Gitelis S, Hartjen C, Watson JT, Kim PT. The use of a surgical grade calcium sulfate as a bone graft substitute: results of a multicenter trial. *Clin. Orthop.* 2001:42–50.	161
43	Fuchs B, Dickey ID, Yaszemski MJ, Inwards CY, Sim FH. Operative management of sacral chordoma. J. Bone Joint Surg. Am. 2005;87:2211–2216.	160
44	Greenspan A. Benign bone-forming lesions: osteoma, osteoid osteoma, and osteoblastoma. Clinical, imaging, pathologic, and differential considerations. Skeletal Radiol. 1993;22:485–500.	160
45	Kneisl JS, Simon MA. Medical management compared with operative treatment for osteoid-osteoma. *J. Bone Joint Surg. Am.* 1992;74:179–185.	160
46	Tang N, Song W-X, Luo J, Haydon RC, He T-C. Osteosarcoma development and stem cell differentiation. Clin. Orthop. 2008;466:2114–2130.	160
47	Coley WB. The treatment of malignant tumors by repeated inoculations of erysipelas. With a report of ten original cases. 1893. Clin. Orthop. 1991:3–11.	157
48	Pritchard DJ, Dahlin DC, Dauphine RT, Taylor WF, Beabout JW. Ewing's sarcoma. A clinicopathological and statistical analysis of patients surviving five years or longer. *J. Bone Joint Surg. Am.* 1975;57:10–16.	155
49	Wise JJ, Fischgrund JS, Herkowitz HN, Montgomery D, Kurz LT. Complication, survival rates, and risk factors of surgery for metastatic disease of the spine. Spine. 1999;24:1943–1951.	152
50	Berrettoni BA, Carter JR. Mechanisms of cancer metastasis to bone. *J. Bone Joint Surg. Am.* 1986;68:308–312.	152

Table 2. Levels of Evidence of the Top 50 Most Cited Articles in Orthopaedic Oncology by Decade

Level of Evidence	Time Period	1	2	3	4	5	Review Article	Basic Science
	1966-1979							
Number of Publications		0	0	2	41	4	2	1
Percentage (%)		0	0	4	82	8	4	2
	1980-1989							
		0	0	7	34	1	8	0
		0	0	14	68	2	16	0
	1990-1999							
		1	2	10	33	0	3	1
		2	4	20	66	0	6	2
	2000-2009							
		0	5	12	21	0	8	4
		0	10	24	42	0	16	8
	2010-2016							
		0	3	16	19	0	4	8
		0	6	32	38	0	8	16

PAPER 39

An Update on the Transcutaneous Osseointegration Experience in the United States

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Transcutaneous osseointegration has recently become an option for those with the more challenging, proximal amputations in the United States. Advantages of the procedure over traditional amputation with an exterior prosthesis include the avoidance of complications related to the socket-skin interface as well as regaining some proprioception in the residual limb. Since 2012, 15 patients have undergone implantation of transcutaneous prostheses, 14 transfemoral and one transhumeral with two further transfemoral procedures planned. This initial cohort of patients was predominantly male and ranged in age from 33 to 68. Reasons for prior amputations include trauma, infection, and cancer. Initially, patients underwent two-stage surgery with implantation and integration happening prior to exteriorization of the prosthesis; the remaining patients underwent single-stage surgery with implantation and exteriorization occurring in the same procedure. There have been six complications requiring revision, four periprosthetic fractures (two in the same patient) and two soft tissue management issues. One of the patients with soft tissue issues also had a taper mismatch requiring component exchange. Revision after fracture has demonstrated improved bone quality over the index procedure, likely a result of the high compressive forces applied by the compress. Currently, use has been limited by FDA regulations. There remain questions about the utility of these prostheses in patients at higher risk of infection or wound healing complications, such as vasculopathic patients or patients with diabetes. Ongoing research at UPMC involves examining the interface between the residual limb and the prosthesis in collaboration with the biodynamics laboratory, with further plans to analyze the gait of transfemoral amputees. Transcutaneous osseointegration represents an exciting new option in the algorithm for treating patients with proximal amputations.

PAPER 40

Targeted Muscle Reinnervation: A strategy to prevent neuroma and phantom limb pain in oncologic amputees

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Background: Malignancy accounts for only 2% of amputations performed in the United States; however, amputation remains a cornerstone in the operative treatment of extremity tumors. Amputation is associated with various limitations on activities of daily living. Adjusting to and coping with these changes and potential mobility challenges can contribute to further physical and psychological morbidity. Despite advancements in prosthetic design affording amputees greater function, residual limb pain affects an amputee's motivation and ability to tolerate and utilize a prosthesis, which can have an immense impact on their function and quality of life.

Neuromas and phantom limb pain (NPLP) are common causes of residual limb pain in the general amputee population, as well as patients undergoing amputation for oncologic diagnoses. These oncology patients in particular experience high rates of phantom limb pain and associated poor prosthetic.

Current treatment for NPLP yields inconsistent and incomplete relief. A novel strategy to address and prevent NPLP in amputees is targeted muscle reinnervation (TMR). TMR is the transfer of transected residual peripheral nerves to otherwise redundant target muscle motor nerves. This is thought to prevent symptomatic neuromas and phantom limb pain and allow for enhanced bioprosthetic function by reestablishing a neural pathway that provides a new functional output for the amputated nerve.

Purpose: This study seeks to determine the preliminary results of the effectiveness of TMR in preventing early symptomatic neuroma formation and phantom limb pain (NPLP) and its effect on the timing of prosthetic use in patients undergoing amputation for oncologic diagnoses.

Patients and Methods: All patients undergoing amputation with simultaneous TMR for the treatment of malignant diagnoses at a large, academic medical center between April 2015 and March 2017 were included. Patient demographics, oncologic characteristics, and adjuvant treatments were noted. The incidence of post-operative wound complications, neuroma and phantom limb pain, and time to prosthetic use were recorded.

Results: Sixteen patients have undergone amputation with concomitant targeted muscle reinnervation for the treatment of an extremity-based malignancy. Six amputations were performed at the index resection. The remaining eleven patients underwent secondary amputation for local recurrence or residual positive margins after primary excision. Phantom limb pain was reported in 62.5% (10/16) at one month, 26.7% (4/15) between one and three month, 33.3% (4/12) between three and six month, and 20% (1/5) at greater than 12 month follow-up. To date, patients undergoing amputation with TMR have yet to present with a symptomatic neuroma. The rate of prosthetic use in patients with greater than one month follow-up was 60% (9/15), with patients beginning prosthetic wear at an average of 3 months. Wound complications

requiring a return to the operating room occurred in 12.5% (2/16) of patients. Patient demographics and outcomes are reported in Table 1.

Conclusion: Targeted muscle reinnervation is an effective strategy to reduce residual limb pain secondary to neuroma formation and phantom limb pain and is associated with high rates of prosthetic use. Interestingly, we have anecdotally noted trends towards earlier cessation of narcotics in our primary TMR cohort, a finding reflected in our non-oncology cohort of patients undergoing amputation with concurrent TMR. Our results suggest that targeted reinnervation is an effective approach in the prevention of painful neuroma and phantom limb pain. Targeted muscle reinnervation has the potential to positively impact the amputee population through improved prosthetic use, neuropathic pain control, decreased narcotic consumption and improved activities of daily living. Long-term follow-up focusing on functional outcomes and narcotic use will be crucial in determining the durability of targeted muscle re-innervation in this patient population.

Table 1:

Level of amputation, age, incidence of neuroma and phantom limb pain, time to prosthetic fitting, primary diagnosis and adjuvant therapies in patients undergoing amputation with TMR. Abbreviations: chemotherapy (CTX), radiation therapy (XRT), pigmented villonodular synovitis (PVNS).

	Level	Age (yrs)	Neuroma Report Follow-Up Interval (mos)					Phantom Limb Pain Report Follow-Up Interval (mos)					Time to Prosthetic (mos)	Oncologic Diagnosis	Adjuvant Therapy			
			1	1-3	3-6	12	>12	1	1-3	3-6	12	>12			Pre-Operative		Post-Operative	
															CTX	XRT	CTX	XRT
1	AKA	11	No	No	No	No	No	Yes	No	No	No	No	2	Osteosarcoma	Yes	-	Yes	-
2	Trans-radial	50	No	No	No	No	No	Yes	No	No	Yes	Yes	6	Synovial Sarcoma	-	-	Yes	-
3	BKA	43	No	No	No	No	No	Yes	No	No	No	No	2	Leiomyosarcoma	Yes	-	-	-
4	Forequarter	59	No	No	No	No	No	No	No	Yes	No	No	-	Chondroblastic Osteosarcoma	Yes	-	Yes	-
5	BKA	33	No	No	No	*N/A*		No	No	No	*N/A*		-	Clear Cell Sarcoma	-	-	-	-
6	BKA	19	No	No	No	No		Yes	No	No	No	No	3	Ewing Sarcoma	Yes	-	Yes	-
7	AKA	52	No	No	No	*N/A*		Yes	No	No	*N/A*		3	Recurrent Malignant Peripheral Nerve Sheath Tumor	-	-	Yes	Yes
8	AKA	51	No	No	No	*N/A*		Yes	Yes	Yes	*N/A*		4	Recurrent PVNS	-	-	Yes	-
9	Forequarter	62	No	No	No	*N/A*		No	No	No	*N/A*		-	Metastatic Colonic Adenocarcinoma	Yes	Yes	Yes	Yes
10	AKA	45	No	No	No	*N/A*		Yes	Yes	Yes	*N/A*		2	Pseudomyogenic Hemangio-endothelioma	-	-	Yes	-
11	BKA	70	No	No	No	*N/A*		Yes	Yes	No	*N/A*		4	Synovial Sarcoma	-	-	-	-
12	AKA	45	No	No	No	*N/A*		No	No	No	*N/A*		-	Recurrent Squamous Cell Carcinoma	-	-	Yes	-
13	BKA	51	No	No	*N/A*			Yes	Yes	*N/A*			2	Clear Cell Sarcoma	-	-	-	-
14	AKA	84	No	No	*N/A*			No	No	*N/A*			-	High-grade Myxofibrosarcoma	-	-	-	-
15	Forequarter	55	No	No	*N/A*			Yes	No	*N/A*			-	Osteosarcoma	Yes	-	Yes	-
16	Forequarter	67	No	*N/A*				No	*N/A*				-	Undifferentiated Pleomorphic Sarcoma	-	Yes	-	-

PAPER 41

F-18 FDG PET Differentiation of Benign from Malignant Chondroid Neoplasms: A Systematic Review of the Literature.

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Background: Differentiation among chondroid neoplasms of bone continues to pose problems for both radiologists and orthopedic oncologists. Treatment options vary depending on the grade of these lesions; including observation up to wide local excision with or without reconstruction. Clinically, these neoplasms show non-specific symptoms, and present overlapping radiologic features across imaging modalities (radiography, CT, TC99m bone scintigraphy, and MRI). Also, the underlying heterogeneity of these tumors makes them susceptible to under sampling. 18F- FDG PET-CT offers direct assessment of tumor metabolic activity, and there has been preliminary investigations into the value of this imaging modality in distinguishing among chondral lesions; however, these studies have been conducted with relatively small sample sizes.

Questions/Purposes: Can 18F- FDG PET-CT aid in:

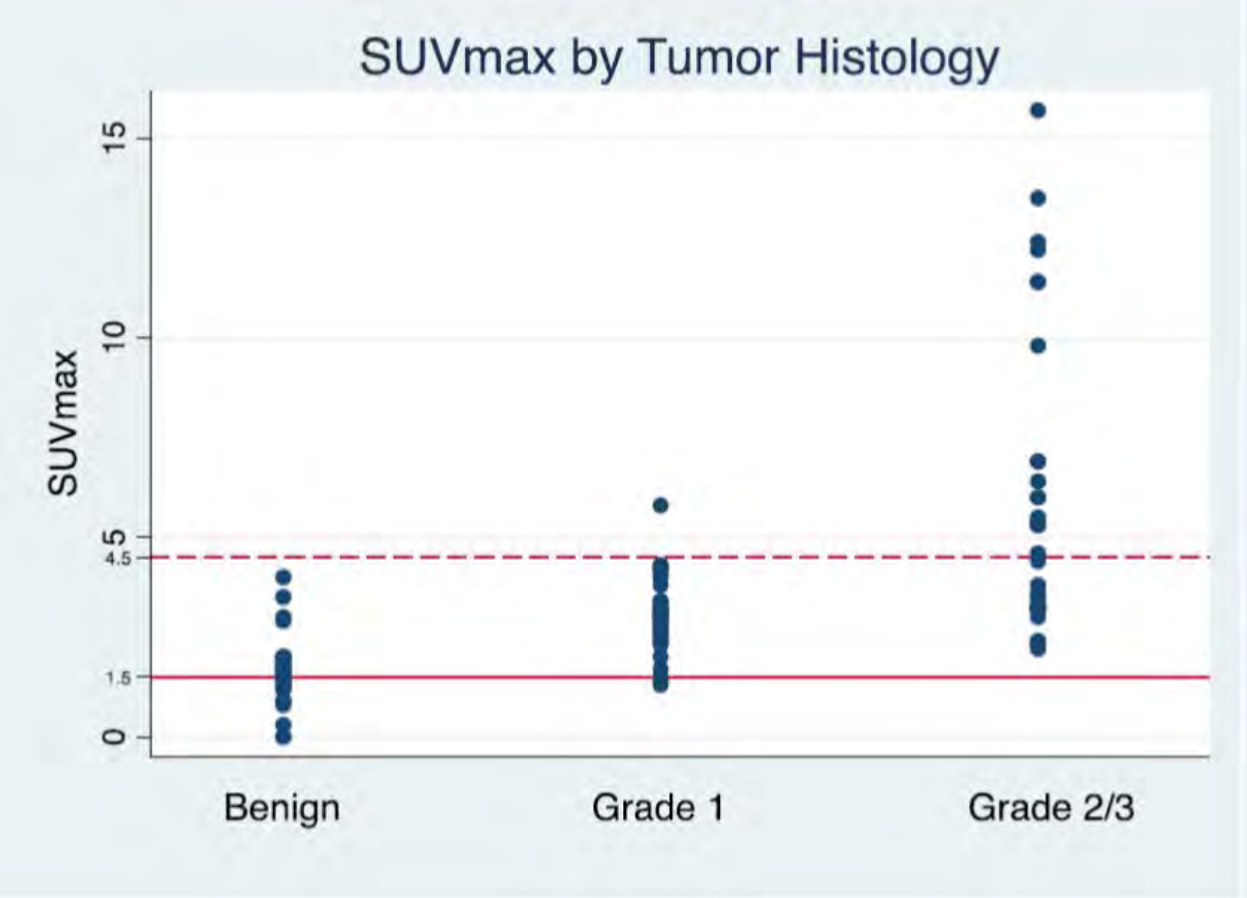
1. Differentiating among the nature of chondral tumors: Benign vs Malignant.
2. Differentiating between benign chondral tumor and low grade chondrosarcomas.

Patients and Methods: A systematic review of the literature was performed identifying 811 PubMed- and EMBASE- indexed articles containing combinations of "chondrosarcoma","enchondroma","chondroid","cartilage", and "PET/CT", "PET", "Positron". Eleven (11) articles including 174 lesions were included. Age, gender, tumor size, histologic grade, and SUVmax values were extracted for individual lesions when possible, and otherwise recorded as aggregated data. Comparisons in SUV max among benign, low-grade, and intermediate/high-grade chondroid neoplasms were made. Demographics were compared among subjects with

available individual data, and differences between those with benign and malignant tumors were assessed using Fisher exact tests and two-sample t-tests. Funnel plots were generated to asses for publications bias (Comprehensive Meta-Analysis,v.3,Biostat Englewood ,NJ,USA). Statistical analysis was performed using Stata 13.1 (StataCorp, College Station, TX, USA). For all analyses, results were considered statistically significant for $p<0.05$.

Results: There were a total of 174 chondroid neoplasms identified in 11 articles which met inclusion criteria (Table 1). Of these, individual SUV max was available for 107 subjects (8 articles). There were 68 benign (osteochondroma or enchondroma), and 106 malignant tumors (45 low-grade, and 61 intermediate/high grade chondrosarcomas) as aggregated data. Funnel plot was constructed and showed no significant publication bias among the 11 selected manuscripts (I^2 = 12.8). Individual data showed 36 benign and 71 malignant lesions; 60 females, and 38 males, with a mean age of 46.6 (range 19-85 years). Malignancy was associated with female gender ($p=0.03$, fisher exact); but neither with age nor size of the lesions. Aggregated data analysis showed a mean SUV max of 1.7 std dev 0.8 for benign tumors vs 4.8 std dev 3.1 for chondrosarcomas ($p<0.0001$, unpaired t-test). SUV max correlated with histologic grade (Spearman $\rho=0.77;p<0.0001$), as mean SUV max showed incremental increases (3.0 (grade 1); 4.7 (grade 2); and 9.3 (grade 3), respectively). Below SUV max of ≤ 1.5 there was a 94% specificity for benign tumors; and above an SUV max of 4.5 there was a 99% specificity in identifying grade 2/3 chondrosarcomas (Figure 1).

Conclusions: 18F- FDG PET-CT could serve as a useful adjunct in differentiating between benign and malignant chondral tumors. Also, there is a correlation within the chondrosarcomas grades. Low SUV max (≤ 1.5) is almost found in benign lesions, while higher SUV max (≥ 4.5) strongly suggests an intermediate/high grade chondrosarcoma. There is a wide “gray zone” with overlapping SUV max between benign and low-grade chondrosarcomas, mainly due to variations in pathology interpretations as well as 18F- FDG PET-CT inherent test variations.



PAPER 42

Management of recurrent desmoid fibromatosis of the upper extremity

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Background: Desmoid fibromatosis of the upper extremity is a challenging clinical entity, because wide surgical resection often proves difficult and recurrence rates are high. Radiation therapy is frequently employed at our institution in cases of recurrence, though the optimal management strategy remains unclear.

Questions/Purposes: We present a cohort of patients treated for recurrent desmoid fibromatosis of the axilla and upper extremity. We sought to assess the impact of radiation and/or additional surgery on local control.

Patients and Methods: Patients treated for upper extremity and axillary desmoid tumors since 1991 at our institution were identified through clinical, operative, and pathology reports, and retrospectively reviewed. Tumors of the hand were excluded. Fisher's exact test was used to compare the rates of re-recurrence and presence of residual / recurrent disease at final follow-up across treatment groups.

Results: We identified 32 patients; minimum follow-up of approximately 1 year was available for 28. Tumors were present in the forearm, upper arm / shoulder, and axilla in 3, 18, and 7 patients, respectively. The initial management of primary disease took place at our institution in 9 cases and at outside hospitals in the remainder, and included surgery alone for 24 patients and surgery plus radiation for 4. Index procedure surgical margins were positive for 13 patients, negative for 6, and unknown for 9. Average age at initial presentation was 37 years, and age at time of treatment for recurrence was 41 years. Patients treated with surgery for recurrence were noted to have had larger tumors at initial presentation (Table 1). Ten patients received hormonal or cytotoxic chemotherapy either before or after treatment for recurrence; regimens and timing varied widely (Table 2).

The initial treatment of recurrent disease included radiation therapy in 19 of 28 patients. Specifically, management consisted of surgery alone in 6 patients, surgery plus radiation in 15,

radiation alone in 4, and observation or medical management only in 3. Margin status is outlined in Table 1. Among patients treated with surgery plus radiation, the average radiation dose was 53 Gy, as compared with 56 Gy among patients in the radiation only group. In cases of surgery plus radiation, timing was as follows: neoadjuvant and adjuvant in 6 patients each, intraoperative brachytherapy in 2, and unknown in 1.

Excluding patients for whom recurrent tumors were treated with observation / medical management only, re-recurrence occurred at a statistically-similar rate among all the 3 treatment groups: in 3 patients (50%) treated with surgery alone, 3 patients (75%) treated with radiation alone, and 6 patients (40%) treated with both ($p = 0.55$). Seven patients for whom initial treatment of recurrence involved resection underwent repeat resection for re-recurrence, including 1 patient who received radiation for the second recurrence (but not for the first).

At median final follow-up of 5 years (range, 0.8-24 years), rates of residual / recurrent disease differed significantly across groups, and were lowest in the surgery plus radiation group: 6.7% (1 of 15 patients), 33% (2 of 6 patients), and 75% (3 of 4 patients), respectively, among those for whom initial treatment of recurrence consisted of surgery plus radiation, surgery alone, or radiation alone ($p = 0.01$).

Conclusions: In this series of 28 patients treated at our institution for recurrent desmoid fibromatosis of the upper extremity, re-recurrence rates were high regardless of treatment (surgery plus radiation, 40%; surgery alone, 50%; radiation alone, 75%). However, there were significant differences between groups with respect to disease status at median 5 year final follow-up: 14 of 15 (93.3%) patients for whom initial treatment of recurrence consisted of both surgery and radiation were disease-free, as compared with 4 of 6 patients (67%) treated with surgery alone and 1 of 4 patients (25%) treated with radiation alone, though 5 patients in the surgery plus radiation group required multiple resections.

These data demonstrate that in the treatment of recurrent upper extremity desmoids, high rates of local control can be achieved by combining surgery and radiation, though multiple resections may be required. However, the functional and oncologic benefit of achieving disease-free status and the potential role for medical management remain unclear.

Table 1.

	n	Age	Tumor vol. (cm^3) on present.†	Location	(+)/(-) Margins on initial resection†	(+)/(-) Margins on resection for recurrence	Re-recurrence	Subsequent treatment for re-recurrence	Residual tumor at final follow-up
XRT	19								
XRT alone	4	42	183	Forearm (2); shoulder (1); axilla (1)	3 / 0	--	3	0	3
XRT + Surg	15	43	321	Upper arm / shoulder (12); axilla (2); forearm (1)	7 / 2	10 / 4	6	Surgery (5)	1
No XRT	9								
Surg alone	6	38	391	Axilla (4); upper arm / shoulder (2)	2 /2	2 / 3	3	Surgery (1), Surgery + XRT (1)	2
Obs/ med	3	39	87	Upper arm / shoulder (3)	1 / 2	--	3		3
*p-value**							*NS*		*0.01*

†Tumor volume at initial presentation (*i.e.*, time of diagnosis of desmoid tumor). Data were not available for the entire cohort, as many patients were initially treated at outside institutions.
*Fisher's exact test was utilized to compare rates of re-recurrence and presence of residual tumor at final follow-up across the XRT alone, XRT + surgery, and surgery alone groups.

Table 2.

	Add'l treament with chemotherapy* (n)	Details (n)
XRT		
XRT alone (n=4)	1	Tamoxifen after 1st resection (1)
XRT + Surg (n=15)	5	Tamoxifen prior to (2) or after (1) resection for recurrence; vinblastine, methotrexate, and hydroxyurea prior to resection for recurrence and imatinib after resection for recurrence (1); doxorubicin after index resection, notch signaling inhibitor after resection for recurrence (1)
No XRT		
Surg alone (n=6)	3	Doxorubicin and tamoxifen prior to index resection (1); imatinib prior to index resection (1); tamoxifen after resection for recurrence (1)
Obs/med Only (n=3)	1	Sorafenib and vinorelbine

*Cytotoxic or hormonal agents

PAPER 43

"Is Surgery Justified in Aggressive Fibromatosis If We Are Supposed To Live Along With It?" Treatment Outcomes in 51 Patients

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Aggressive fibromatosis (AF), a.k.a. desmoid tumor, is the benign agressive fibroblastic proliferation of bone and soft tissues, which characterized by infiltrative growth and higher risk of local recurrence even after wide surgical margins. Some lesions may demonstrate spontaneous regressions with watchful waiting. The local control of AF is challenging for orthopaedic oncologists thus radiotherapy and chemotherapy was found effective pre and/or postoperatively. Non-steroid anti-inflammatory drugs (NSAID) are also reported to be effective. The purpose of this study is to evaluate recurrence free and overall survival of extraabdominal AF, which surgically treated and followed up by single surgeon, with the analysis of surgical margins and influence of postoperative additional treatment modalities.

We retrospectively reviewed the data of 51 patients (23M/28F) who underwent surgery with the histopathologic diagnosis of extraabdominal aggressive fibromatosis in our institute. The patients were evaluated regarding age, localizations, compartmental involvement, status of the lesion at the time of first referral (primary/recurrence) and tumor volume. The type of resection, histopathological margins (R0,R1,R2), the use of neoadjuvant or adjuvant treatment (chemotherapy, radiotherapy, tamoxifen or NSAID), postoperative complications and recurrences were also noted. The authors' method for protection of the major neurovascular structures by synthetic vascular graft sheath use was noted. The oncological status, overall survival and recurrence-free survival were evaluated.

Mean age was 24,1 (2-56), and most common localizations were popliteal (13,7%) and thigh (11,8%) region. In 91,5% of the patients the lesions had extra-compartmental extensions. Most of the lesions in this study (58,8%) were primary lesions. Although wide resection was the most commonly applied method for resection (94,1%), histopathological margins were negative in only 52,9% and closer than 1 mm in 19,6% of the cases. The mean tumor volume was 451 cm^3 (2-1650). Three patients received chemotherapy, elsewhere hospital (imatinib, methotrexate, ifosfamide, mesna, doxorubicin), 24 patients received radiotherapy (30-54 Gy), 11 patients were prescribed long-term meloxicam and 2 received tamoxifen.

Postoperative complications were encountered in 37,3% of the patients. Postoperative complications were significantly higher in patients with recurrent AF at first referral when compared to primarily diagnosed AF ($p<0,05$). Recurrence or progression after surgery was observed in 66,7% of the patients within a mean time of 21 months. The lesions greater than

100 cm^3 tend to recur significantly when compared to the lesions smaller than 100 cm^3 ($p<0,05$). The mean volume of the lesions in patients who received RT was 315,5 cm^3 (23,1-825). 41,2% of the lesions were recurrent at their first referral, 30 cases recurred at least once and mean time to recurrence was 24,9 months (2-108). Second recurrences were evaluated in 18 patients (mean 25,2 months), third recurrences in 6 (mean 17 months) and fourth recurrence in 1 patient (6 months). In our series 70,2% of the patients were CDF or NED. The mean recurrence free survival was 51,8 months.

Surgery is still the treatment of choice in desmoid tumor patients, which are resectable with acceptable morbidity. Due to benign nature of the disease, possibility of spontaneous regression and high local recurrence rate despite truly wide margins, radical surgical interventions involving sacrification of vital structures should be avoided. Patients requiring morbid resections should strongly be considered for treatment with adjuvant agents. The patients should be well informed that aggressive fibromatosis is “a disease to live together with”.

PAPER 44

High Local Recurrence Rate For Giant Cell Tumor Of Bone After Neoadjuvant Denosumab Treatment

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Background: Giant cell tumor of bone makes up approximately 3-5% of all primary bone tumors and is commonly found directly under the joint surface. The standard therapy is a curettage, adjuvant treatment, and filling the defect with either bone cement or allograft bone. This has a reported local recurrence rate of 20-50%. A second treatment option is resection of the joint and reconstruction either as a fusion or total joint arthroplasty. This has a reported local recurrence rate of 5-20%.

Overexpression of receptor activator of nuclear factor kappa-B ligand (RANKL) by neoplastic stromal cells has been implicated in the pathogenesis of giant cell tumor of bone. Denosumab is a fully human monoclonal antibody that targets RANKL. Denosumab was approved by the FDA in June 2013 for treatment of giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity. Since its original release, reports have shown that the extent of surgery can be significantly reduced with salvage of the native joint when denosumab is utilized as a neoadjuvant treatment. However, the risk of local recurrence using this strategy remains unknown.

Purpose: The primary aim of this study is to determine the local recurrence rate after neoadjuvant denosumab and curettage for giant cell tumor of bone. The secondary aim is to determine whether neoadjuvant denosumab would aid in preservation of the native joint.

Methods: A retrospective chart review was performed evaluating all patients who received neoadjuvant denosumab treatment for giant cell tumor of bone followed by curettage of the lesion. Date of diagnosis, number of denosumab treatments, date of surgery and type of surgical treatment were reviewed. In addition, if there was a recurrence, date of diagnosis, date of surgery, and type of surgical treatment were reviewed.

Results: Between 2013 and 2016, five patients were identified as being treated with neoadjuvant denosumab. These patients had significant destruction of subchondral bone for which the optimal surgical treatment was wide resection followed by fusion, arthroplasty, or amputation. Denosumab was administered in 3 weekly loading doses followed by 4-5 monthly

maintenance doses. Surgery was performed 6 months after the first loading dose. All 5 patients received curettage of the lesion followed by argon beam coagulation and allograft packing at the subchondral bone. Four patients had polymethymethacrylate (PMMA) placed in the defect. Two patients had plate stabilization.

Four of 5 patients (80%) had local recurrence an average of 19 months (range 7-29 months) after curettage. The fifth patient is 3 months postoperative. The subsequent procedures performed on 3 patients included wide resection: one required wrist fusion, one underwent distal femur replacement, and one had a below knee amputation. The fourth patient had repeat curettage and allograft packing. Of these 4 patients, none have had a local recurrence in initial follow-up (mean 2 month, range 0-3).

Conclusions: Despite initial results, neoadjuvant denosumab ultimately did not enable long-term joint preservation. There appears to be an unacceptably high recurrence rate when utilized as neoadjuvant treatment. In this series, denosumab delayed the original planned surgery by 1-2 years, resulting in patients undergoing two operative procedures. One possible reason for the high local recurrence rate is that preoperative use may limit the ability to recognize active disease and perform adequate curettage. It is likely that to preserve a native joint in severe cases, denosumab may need to be used as a lifetime medication for disease control, and the risks of prolonged usage are unknown.

PAPER 45

A Comparison of Outcome of Treatment Paradigms for Sacral Chordoma: Does Preoperative Radiation Improve Prognosis?

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Background: The mainstay of treatment for sacrococcygeal chordomas is en-bloc excision with negative margins; however this often leads to significant morbidity for patients. Even following complete surgical resection there remains a high rate of local recurrence. As such, some institutions combine preoperative radiotherapy with surgical excision in an attempt to reduce the risk of local recurrence in the setting of the close resection margins which are inherent to these procedures.

Purpose: The purpose of this study was to compare cohorts from three large tertiary sarcoma centers in North America (USA and Canada) to determine if the addition of preoperative radiotherapy to the treatment protocol for patients with chordoma can improve outcomes, with a specific focus on (1) overall survival; (2) recurrence free survival; and (3) postoperative complications.

Methods: We identified 176 patients who underwent surgical excision of a primary sacrococcygeal chordoma at our institutions from 1990-2015. There were 62 females and 114 males, with a mean age of 57 years at the time of surgery and a mean follow-up of 7 years (range 1 to 25 years). All patients underwent resection with curative intent. Negative margins were obtained in 147 (84%) patients. The common most cephalad resection level was S2 (n=56). Neoadjuvant radiotherapy was given to 91 patients, with a mean dose of 42 Gy. There was no difference in the mean age (P=0.96), proportion of males (P=1.0), mean tumor volume (P=0.23), proportion of high sacral resections (P=1.0) and proportion of positive margins (P=0.32).

Results: The 10-year recurrence-free and overall survival was 50% and 61%. Patients with a tumor size greater than 9 cm in maximal dimension was associated with increased risk of mortality (HR 1.94, P=0.03) and disease recurrence (HR 2.16, P=0.03). Local recurrence occurred in 30 patients, with a 10-year local recurrence free survival of 77%. A positive surgical

margin (R1 or R2) was associate with local tumor recurrence (HR 2.37, P=0.03), likewise local recurrence was associated with metastatic disease (HR 3.36, P<0.001).

Postoperative complications occurred in 54% of patients; most commonly wound break down (n=104) and sacral insufficiency fracture (n=26).

Preoperative radiotherapy did not reduce the risk of mortality (HR 1.59, P=0.14), local recurrence (HR 0.66, P=0.27), or development of metastatic disease (HR 0.94, P=0.87). However, preoperative radiotherapy did increase the risk of postoperative wound complications (HR 2.40, P<0.001) and sacral fracture (HR 4.40, P<0.001).

Conclusion: The ability to achieve a negative margin and tumor size were the most important factors in the surgical treatment of sacral chordomas in terms of mortality and local recurrence. In this retrospective study, preoperative radiotherapy did not reduce the risk of mortality, local tumor recurrence or distant disease. It was however associated with a significantly increased risk of wound complications and sacral fracture.

Table 1: Factors Affecting Overall- and Disease Free Survival Following Surgical Excision of a Sacral Chordoma

Patient Factors	**Overall Survival Hazard Ratio (95% CI)**	***P Value***	**Disease Free Survival Hazard Ratio (95% CI)**	***P Value***
Local Tumor Recurrence	1.65 (0.87-3.04)	0.11	-	-
Metastatic Disease	**1.97 (1.01-3.83)**	**0.04**	-	-
Positive Surgical Margin	**0.92 (0.37-1.95)**	**0.84**	1.25 (0.50-2.75)	0.59
Males	1.38 (0.73-2.75)	0.31	1.68 (0.79-4.01)	0.17
Age ≤ 55 Years	0.69 (0.36-1.26)	0.23	1.35 (0.68-2.70)	0.38
Tumor Dimension ≥9 cm	1.94 (1.04-3.68)	0.03	**2.16 (1.05-4.55)**	**0.03**
Tumor Volume ≥460 cm^3	1.64 (0.87-3.05)	0.12	1.52 (0.51-2.42)	0.71
Preoperative Radiotherapy	1.59 (0.85-3.01)	0.14	0.89 (0.43-1.79)	0.75
High Sacral Resection	1.29 (0.66-2.66)	0.45	1.87 (0.90-4.15)	0.09
Patient Factors	**Local Disease Free Survival Hazard Ratio (95% CI)**	***P Value***	**Distant Disease Free Survival Hazard Ratio (95% CI)**	***P Value***
Local Tumor Recurrence	-	-	**3.36 (1.64-6.70)**	**0.001**
Positive/Marginal Surgical Margin	**2.37 (1.06-4.95)**	**0.03**	1.22 (0.49-2.68)	0.63
Males	0.93 (0.44-2.02)	0.84	1.72 (0.81-4.08)	0.16
Age ≤ 55 Years	1.23 (0.59-2.54)	0.56	1.34 (0.67-2.67)	0.39
Tumor Dimension ≥9 cm	1.02 (0.47-2.15)	0.95	2.07 (1.01-4.37)	0.04
Tumor Volume ≥460 cm^3	0.65 (0.25-1.47)	0.31	1.11 (0.49-2.35)	0.77
Preoperative Radiotherapy	0.66 (0.30-1.38)	0.27	0.94 (0.46-1.88)	0.87
Postoperative Radiotherapy	1.02 (0.48-2.12)	0.94	0.97 (0.46-1.96)	0.95
High Sacral Resection	1.25 (0.59-2.76)	0.55	1.82 (0.88-4.03)	0.10

PAPER 46

Clinical Outcomes of Vascularized Fibular Graft for Treatment of Late Radiation-Induced Complications in Long Bones

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Background

Radiation therapy (RT) is used as an adjuvant therapy for local control of soft tissue sarcomas of the extremitiess and historically has been considered the definitive local treatment for Ewing sarcoma. Early RT complications include wound dehiscence, hematoma formation, and infection. Long-term complications include neurological dysfunction, soft tissue fibrosis, skin scarring, pathological fracture, and non-union, as well as the most serious complication, radiation-induced sarcoma. Radiation-induced fractures managed with internal fixation carry an elevated risk of failure, as fibrosis and devitalization of bone can lead to persistent non-union. The resulting mechanical failures then require further interventions. In such cases, a vascularized fibular graft (VFG), with its inherent blood supply, may be used to enhance union in oncologic patients with late complications of RT to bone and/or soft tissue.

Purposes

We retrospectively analyzed our institutional experience to assess: (1) clinical outcomes (MSTS score, union time, graft hypertrophy and complication incidence) of VFG for treatment of late radiation-associated non-union or reconstruction after resection of radiation sarcoma; (2) the correlation between onset and dose of RT and the extent of local tissue fibrosis and scarring; and (3) the effect of radiation-induced soft tissue fibrosis on recipient vessel exploration and the integrity of the performed vascular anastomosis.

Methods

We searched our institutional surgical database to identify oncologic patients with prior history of RT who received vascularized fibular grafts between 1986 and 2014 in conjunction with fixation of pathologic fracture. We identified 13 patients who presented with radiation fracture non-union (n=8), post-radiation local recurrences (n=2), and radiation-induced sarcomas (n=2). Median age was 44 years (range: 17-66) and median follow-up was 75 months (range: 26-298). Primary histologic diagnoses were soft tissue sarcoma (n=7), Ewing sarcoma (n=2), lymphoma (n=2), and desmoid tumor (n=2). The fractures occurred in the humerus (n=6), the femur (n=4) and ulna or radius (n=3). Median radiation dose was 5000 cGy (range: 3500-5050) and the

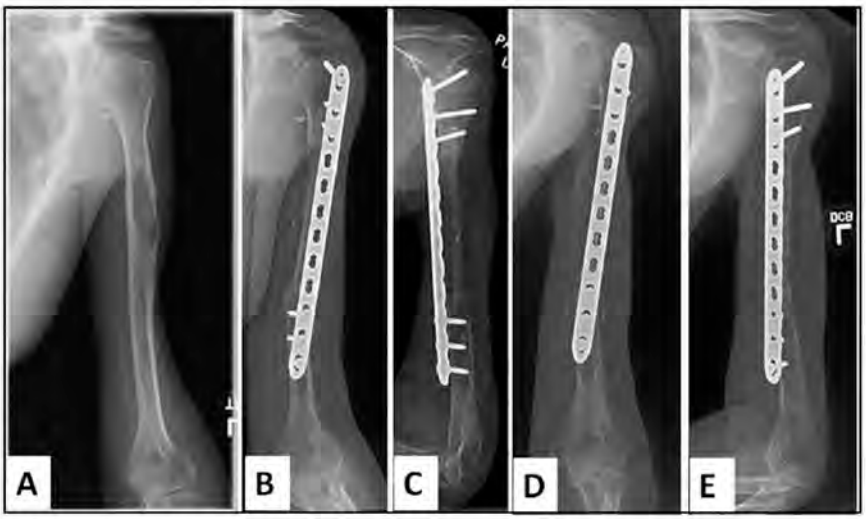
median interval between RT and VFG was 5 years (range: 3-29). Transfer of osteocutaneous VFG was achieved in 8 (62%) patients and osseus flap in 5 (38%). Autogenous iliac graft and/or allograft cancellous bone chips were used in 7 patients (54%) while an electrical stimulation device was inserted in 2 patients (15%). Additional split thickness grafting was required in 4 patients (32%) for adequate wound coverage. ANOVA was used to assess statistical significance.

Results

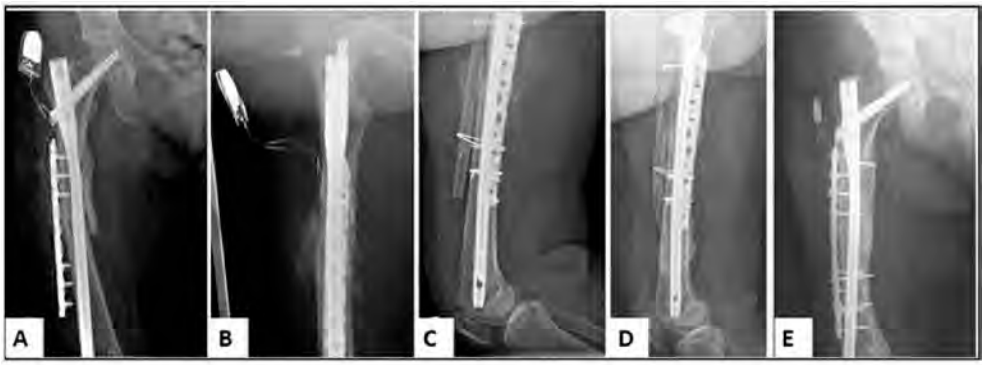
1) Twelve flaps (92%) survived through the last follow-up, and 1 patient underwent above knee amputation 6 months after surgery for chronic osteomyelitis. Radiological union was achieved in 9 patients (70%) and the mean time to union was 22 months (range: 8-29). Mean union time in radiation-induced fractures was 24 months versus 12 months in patients who underwent resection of recurrent tumors or radiation-induced sarcoma (P=0.1). Graft hypertrophy was observed in 4 patients (31%). Median MSTS score was 24 (range: 15-28). Complications included partial skin flap necrosis (n=2; 15%) which required free myocutaneous flap transfer, deep infection (n=2; 15%), and non-union (n=4; 31%). In 6 patients (46%) union was delayed (>24 months); 3 required bone grafting.
2) Intraoperative observations of soft tissue fibrosis were correlated with radiation dose and RT-to-VFG interval. In patients with extensive fibrosis, the mean radiation dose and mean interval between RT and VFG were 5066 cGy and 12 years, respectively, versus 4390 cGy and 3 years for patients with unremarkable soft tissue status. The difference between groups was significant for mean interval between RT and VFG (P=0.04) but not for mean radiation dose (P=0.1).
3) Although soft tissue dissection to explore appropriate recipient vessels was difficult, successful vascular anastomosis was achieved in all patients; for humeral reconstruction, end-to-end anastomosis with a muscular branch from the brachial artery was performed in 4 patients, while the other 2 underwent end-to-side anastomosis with the brachial artery. All arterial anastomoses in the thigh were done in an end-to-end fashion with the circumflex femoral artery. One patient (8%) developed a complication, thrombosed venous anastomosis, which required immediate exploration and reanastomosis.

Conclusions

Although surgical treatment of late radiation fracture and non-union is challenging, with historically poor internal fixation outcome, use of VFG in our cohort was associated with good postoperative function and increased union potential at the fracture site. Long RT-to-fracture interval and higher radiation doses were found to be risk factors for local soft tissue compromise, but the degree of compromise in affected patients did not prevent successful intraoperative vascular exploration or postoperative anastomosis integrity in most patients. Further studies of this technique with larger patient groups and comparative treatment modalities is warranted.



Case 1: A 32-year-old woman presented with radiation-induced sarcoma in the humerus and was treated with radical resection and reconstruction with vascularized fibular graft. (A) Preoperative radiograph; (B) immediate postoperative radiograph; (C) 10 months after surgery (bone grafting); (D-E) AP and lateral views at 14 months showing full union.



Case 2: A 66-year-old woman presented with femoral radiation fracture and non-union with failure of her previous fixation and graft; she was treated with vascularized fibular graft and minimal internal fixation. (A-B) AP and lateral preoperative radiographs; (B) immediate postoperative radiograph; (D-E) AP and lateral radiographs at 26 months post-surgery, showing full union.

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Computer-Assisted Surgery in Orthopedic Oncology. Indications and Results of 164 procedures.

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Background: Image-guided surgical navigation allows the orthopedic oncologist to perform adequate tumor resection based on fused images. Although surgical navigation was first performed in spine and pelvis, recent reports have described the use of this technique in bone tumors located in the extremities. This technique has moved from localization or percutaneous resection of benign tumors to complex bone tumor resections and guided reconstructions. In recent years, the reported series have increased from small numbers (5 to 16 patients) to larger ones (up to 130 patients). Our aim was to evaluate the efficacy of navigation-assisted surgery for oncologic procedures.

Questions/Purposes: The purpose of this paper was to review our experience regarding surgical navigation, focalized in indications, the results obtained and how problems were solved.

Patients and Methods: We performed a retrospective study of all oncological procedures performed with the assistant of navigation in a single institution from May 2010 to May 2015. During this period 164 procedures were performed with this technique. Seventy-two tumors were located in the femur, 42 in the pelvis, 33 in the tibia, 9 in the sacrum, 6 in the humerus, 1 in the ulna and 1 in the foot. Malignant primary tumors was the primary indication (125), followed by 23 metastasis and 16 benign tumors. We categorized the use of navigation assistance in image-based intralesional treatment, image-based resection and image-based resection and reconstruction.

Results: Based in the indications for navigation only 8 procedures were image-based intralesional treatment, 65 procedures were image-based resection and 91 procedures were image-based resection and reconstruction with allografts. The 8 image-based procedures intralesional were 5 benign tumors (two have recurrence) and 3 metastatic disease (three recurrence). In the 65 image-based resection procedures, 4 were benign lesions (no recurrence), 11 were metastatic disease and 50 were primary bone tumors. The primary location in this group was pelvis and sacrum (50 procedures), followed by 11 femurs, 3 tibia, 2 humerus and 1 foot. In the 91 image-based resection and reconstruction with bone allografts all patients were in long bones (57 femurs, 29 tibias, 4 humerus and 1 ulna). Sixty-one patients were reconstructed with an intercalary allograft (23 hemicylindrical and 38 segmental) and 30 were osteoarticular.

Conclusions: Although, image based intralesional treatment had been described as an indication for navigation, we find high recurrence rate. Image-based resections were mainly performed in pelvis and sacrum. Image-based resection and reconstruction were performed when a reconstruction with bone allograft was planned. In conclusion, in our series the main indications for navigation were primary malignant tumors and the main use was image-based resection for pelvic and sacrum tumors and image-based resection and reconstruction for long bones tumors reconstructed with bone allograft.