Complications following allograft reconstruction for primary bone tumors: Considerations for management☆

Joseph A. Ippolito, Maximilian Martinez, Jennifer E. Thomson*, Alexander R. Willis, Kathleen S. Beebe, Francis R. Patterson, Joseph Benevenia

Rutgers New Jersey Medical School Department of Orthopaedics, 140 Bergen Street, ACC D1610, Newark, NJ, 07103, USA

ABSTRACT

Introduction: The aim of this study was to investigate complication rates and types following allograft reconstruction and discuss unique considerations for management.

Methods: Seventy-four consecutive patients underwent large segment allograft reconstruction following resection of primary musculoskeletal tumors from 1991 to 2016. Mean patient age was 32 ± 20 years (range, 5–71 years). Minimum follow-up was 2 years unless patients were lost to disease prior. Mean follow-up was 105 months.

Results: Thirty-five patients had complications requiring subsequent surgery at a mean of 30 months (range, 1–146 months) post-operatively. Individual complication rates were 29%, 50%, and 42% for Allograft Prosthetic Composite, Intercalary, and Osteoarticular allograft reconstruction, respectively. Risk factors for complication included age less than 30 (OR 4.5; $p = 0.002$), male gender (OR 2.8; $p = 0.031$), chemotherapy (OR 4.4; $p = 0.003$), lower extremity disease (OR 3.4; $p = 0.025$). In patients with complications, limb-retention rate was 91% and mean MSTS scores were 23.6.

Conclusion: Despite considerable complication rates, management with a systematic approach results in successful outcomes with limb-retention greater than 90% and mean MSTS scores of 79%. In carefully selected patients, allografts provide a reliable method of reconstruction with treatable complications occurring at a mean of 30 months.

1. Introduction

Following tumor resection, large segment allografts are an option for reconstruction of the long bones. A common alternative option for limb salvage is endoprosthetic replacement. Even with numerous advances in endoprosthesis design, reconstruction with intercalary allograft, osteoarticular allograft, and allograft-prosthetic (APC) composite results in good to excellent functional outcomes in carefully selected patients.[1–8] In patients with large diaphyseal lesions, endoprosthetic replacement may be difficult due to limited bone stock for stem fixation proximally or distally. Intercalary allograft offers a reasonable alternative, while preserving bone stock for future procedures, though rates of non-union and fracture remain high.[1,9–12] In cases of tumors growing in close proximity to the joints, reconstruction with osteoarticular allograft to repair a hemi-articular defect can spare the reciprocal joint surface, as well as allow for a more biologic reattachment of nearby tendons.[13,14] However, complication rates as high as 70% have been reported previously.[5,7,8,14–20] Similar to osteoarticular allograft, reconstruction with an APC confers comparable biologic advantages while providing the stability of arthroplasty, despite considerable rates of complications including nonunion.[6,21–24]

Although reconstruction using large segment allograft is associated with risk of complication, successful subsequent management has resulted in successful outcomes and high rates of limb salvage and joint preservation.[1,6,21–27] Previous studies have demonstrated potential benefits of distinct approaches to specific types of graft failure, as well

as unique considerations depending on graft type (intercalary allograft, osteoarticular allograft, or APC). The purpose of this study was to review the management of complications in patients reconstructed with large segment allograft following tumor resection and ask the following questions: (1) Can successful outcomes and satisfactory limb salvage be achieved following complications of allograft reconstruction? (2) Should unique considerations be made for management by complication or allograft type (intercalary, osteoarticular, APC)? In this study, we report on the complications following implementation of large segment allografts following tumor resection and suggest a standardized approach to management.

2. Methods

Following Institutional Review Board (IRB) approval, patients with primary musculoskeletal tumors treated at our institution from 1991 to 2016 were retrospectively reviewed. After chart review, 74 consecutive patients were identified as undergoing reconstruction with intercalary allograft (38), osteoarticular allograft (15), or an allograft-prosthetic composite (21). Pathologic diagnoses included osteosarcoma (24), chondrosarcoma (15), Ewing's sarcoma (9), undifferentiated pleomorphic sarcoma (5), multiple myeloma (5), giant cell tumor (5), adamantinoma (3), aneurysmal bone cyst (3), fibrous bone lesion (2), leiomyosarcoma (1), epitheliod hemangioma (1), and myxoid liposarcoma (1). Mean age was 32 ± 20 years (range, 5–71 years). For all patients, the following characteristics were obtained for analysis: gender, age, diagnosis, and surgical date (Table 1).

Complications were retrospectively grouped by Henderson's failure modes modified for limb salvage with allograft.[28] These modes include soft-tissue failure (Type 1), nonunion at the graft-host junction (Type 2), structural failure (Type 3), infection (Type 4), recurrent disease (Type 5). Functional outcomes were assessed using the MSTS scoring system.[29] Minimum follow-up was 2 years unless patients were lost to disease prior. Mean follow-up was 105 months.

Table 1
Demographic information.

Characteristic	
Age (Mean $\pm$ SD)	32 ± 20 years
Gender (Males, Females)	33, 41
Allograft Type	
Intercalary Allograft	38
Allograft Prosthetic Composite	21
Osteoarticular Allograft	15
Anatomic Location	
Tibia	25
Femur	19
Humerus	16
Pelvis	7
Forearm	7
Pathology	
Osteosarcoma	24
Chondrosarcoma	15
Ewing's Sarcoma	9
Undifferentiated Pleomorphic Sarcoma	5
Multiple Myeloma	5
Giant Cell Tumor	5
Adamantinoma	3
Aneurysmal Bone Cyst	3
Fibrous Bone Lesion	2
Leiomyosarcoma	1
Epithelioid Hemangioma	1
Myxoid Liposarcoma	1
Failure Types	
Type 1 – Soft Tissue Failure	2
Type 2 – Nonunion	17
Type 3 – Structural Failure	6
Type 4 – Infection	5
Type 5 – Recurrence	5

At our institution, three surgeons (JB, FRP, KSB) utilized a standardized approach to managing complications. Compared to previous noteworthy studies from outside the United States,[1,21,25] readily accessible modular and customizable endoprostheses as well as surgeon preference has resulted in a higher propensity to manage allograft complications with conversion to endoprostheses. At diaphyseal bone, modern modular intercalary endoprosthesis designs have aided in successful outcomes,[30] furthering an institutional tendency to pursue endoprosthetic replacement.

Soft-tissue (Type 1) failures in all allograft types were managed with irrigation and debridement, with removal, if necessary, of any protruding hardware. Nonunion (Type 2) in intercalary or osteoarticular allograft were managed initially with supplemental autograft (iliac crest bone graft or vascularized free fibula). Nonunion in patients with allograft-prosthetic composite was managed with conversion to an endoprosthesis. Structural (Type 3) failures in patients with all three graft-types were managed with conversion to endoprosthesis. Infection (Type 4) in all three graft-types was managed initially with a two-stage re-implantation protocol, which included obtaining ESR, CRP, and tissue cultures at time of infection and prior to re-implantation. In the interim period, an antibiotic impregnated spacer was utilized along with the administration of intravenous antibiotics. Patients underwent endoprosthetic replacement upon resolution of infection. Recurrent disease (Type 5) in patients with osteoarticular allograft or APC was managed with subsequent resection and endoprosthetic replacement. Both patients with a complication of intercalary allograft were skeletally immature and managed with resection and repeat intercalary allograft reconstruction.

Analysis of categorical information was performed using a chi-square test, unless an expected value was less than five, in which case Fischer's exact test was utilized. Odds ratios were generated with computation of confidence intervals utilizing the Baptista-Pike method. Analysis of continuous variables was performed using an unpaired t-test when comparing two groups and using a one-way analysis of variance (ANOVA) when comparing three or more groups. All analyses were performed using GraphPad Prism version 7.00 for Mac OS X (GraphPad Software, La Jolla, California, USA, www.graphpad.com). In all tests, significance was set at $p < 0.05$.

3. Results

Of 74 patients with primary musculoskeletal tumors managed primarily with large segment allograft, 35 (47%) patients suffered a complication. Pathologic diagnoses included osteosarcoma (16), chondrosarcoma (6), Ewing's sarcoma (5), adamantinoma (2), aneurysmal bone cyst (2), fibrous bone lesion (2), giant cell tumor (2), and myxoid liposarcoma (1). Complications occurred at a mean of 30.8 months post-operatively, and were comparable ($p = 0.459$) by graft types: intercalary (24.8 months), osteoarticular (43.3 months), and APC (33.7 months) (Fig. 1). Mean graft survival was 51 months and limb retention rate of patients with complications was [32/35 (91%)]. Complication rates were also comparable among patients with intercalary allograft [20/40 (50%)], osteoarticular allograft [8/19 (42%)], and APC [7/24 (29%)]; ($p = 0.263$). Mean overall MSTS scores following treatment of complications were 23.6, and were comparable ($p = 0.394$) by graft type: intercalary (24.5), osteoarticular (24.0), and APC (20.6). MSTS scores following treatment of complications were also comparable ($p = 0.534$) by complication type: soft-tissue failure [29/30 (97%)], nonunion [23.9 (80%)], structural failure [20/30 (67%)], infection [23.2 (77%)], and recurrent disease [23.8 (79%)].

Patients younger than 30 were at increased risk for complication [25/39 (64%) versus 10/35 (29%); odds ratio 4.5; 95% CI, 1.7–11.6; $p = 0.002$]. Patients with complications had a mean age of 24.9 ± 3.1 compared to patients without complications with a mean age of 40.8 ± 3.0. Male patients were at greater risk of suffering complication than female patients [22/33 (67%) versus 17/41 (42%); odds ratio
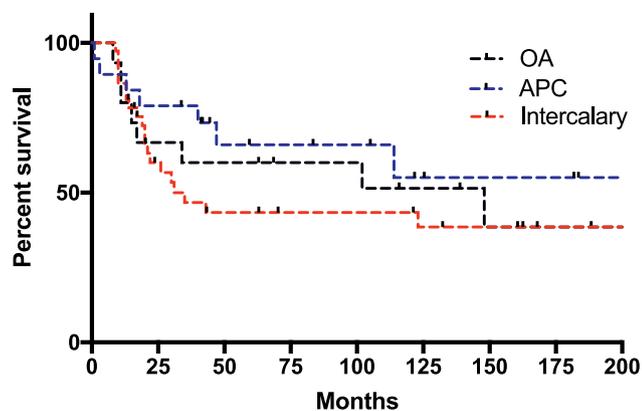
Fig. 1. Kaplan meier survival curve by allograft type.

Table 2
Analysis of factors predicting complication.

Risk Factor	OR (95% CI)	P Value
Age < 30	4.5 (1.7–11.6)	0.002
Male Gender	2.8 (1.1–6.9)	0.031
Chemotherapy	4.4 (1.7–11.3)	0.003
Lower Extremity Disease	3.4 (1.1–10.3)	0.025

*Statistically significant at *p*-value < 0.05.
**Intercalary graft was more likely to suffer nonunion.
Abbreviations: CI (Confidence Interval).

2.8; 95% CI, 1.1–6.9; p = 0.031]. Patients who received chemotherapy were at increased risk for complications [21/31 (68%) versus 14/43 (33%); odds ratio 4.4; 95% CI, 1.7–11.3; p = 0.003]. Complication rates were calculated for the following anatomical locations: Tibia [16/25 (64%)], Femur [11/19 (58%)], Humerus [5/16 (32%)], and Forearm [1/7 (14%)]. Patients were more likely to suffer complication following reconstruction with allograft at the lower extremity compared to the upper extremity [29/52 (56%) versus 6/22 (27%); odds ratio, 3.4; 95% CI, 1.1–10.3; p = 0.025] (Table 2).

3.1. Soft-tissue failures (type 1)

Two cases of aseptic wound dehiscence were seen in the following graft types: intercalary (1) and osteoarticular (1). Following irrigation, debridement, and partial removal of hardware, both patients retained their graft at a mean follow-up of 67 months.

3.2. Nonunion (type 2)

Seventeen type 2 complications were seen in the following grafts: intercalary (13), osteoarticular (1), and APC (3). After treatment with supplemental bone grafting, one patient with osteoarticular allograft, and 8/13 (62%) patients with intercalary allograft were managed successfully, retaining their graft at a mean of 61 months follow-up. After conversion to endoprosthesis, three patients with APC were converted successfully without further complications at a mean of 88 months follow-up. Of the 5 intercalary allograft patients with persistent nonunion after initial supplemental grafting procedure, four were treated with conversion to an endoprosthesis, while one patient opted for a below the knee amputation. These patients have been without further complications at a mean of 109 months follow-up.

3.3. Structural failures (type 3)

Six structural failures were seen in the following graft types: intercalary (2), osteoarticular (2), and APC (2). All were managed successfully with conversion to endoprosthesis without any additional

complications at a mean follow-up of 150 months.

3.4. Infections (type 4)

Five infections were seen in the following graft types: intercalary (2), osteoarticular (1), and APC (2). Four (80%) patients underwent successful two-stage re-implantation without further complications at a mean of 92 months follow-up. One patient with an APC with an infection refractory to treatment with intravenous antibiotics and antibiotic spacer ultimately underwent amputation 43 months post-operatively.

3.5. Recurrent disease (type 5)

Five recurrences of disease were seen in the following graft-types: intercalary (2), osteoarticular (2), and APC (1). All patients were managed successfully with resection and endoprosthetic replacement without further complications at a mean follow-up of 63 months. Two skeletally immature patients with intercalary allograft were initially managed with resection and repeat allograft – both patients experienced subsequent complications. One patient experienced a physeal arrest at the proximal tibia 41 months later. At this time, the patient was near skeletal maturity, and was treated with contralateral epiphysiodesis. Another patient experienced a second recurrence of Desmoplastic Fibroma at the forearm 34 months later. At this time, a decision was made with the patient and family to perform an above the elbow amputation.

4. Discussion

The implementation of allografts in limb salvage procedures allows for the preservation of osseous structures following massive resection with comparable functional outcomes to endoprosthetic reconstruction.[1–8,42,44] Despite the benefits surrounding allograft reconstruction, complication rates such as infection, fracture, and non-union are widely reported.[31,32] Postoperative rates of infection have been reported to range from 0 to 57.8% in the literature (Table 3). Postoperative rates of nonunion and fracture have been shown to range from 0 to 53.3% and from 0 to 77.2%, respectively (Table 3).

In this study, 35 (47%) patients treated primarily with either an intercalary allograft, osteoarticular allograft, or APC experienced a complication. Despite this rate of complication, 77% of patients experiencing a complication were managed with successful limb salvage after one additional procedure and 91% were managed with two or less additional procedures. Most patients with complications in this series suffered them within two years of surgery. In patients with greater than two years follow-up, the complication rate was considerably lower. Similarly, Musculo et al.[16] found a high rate of complications in the short-term postoperative period, while no additional failures occurred after four years and limb salvage rate was 97%.

Intercalary allografts are regarded as easy to implant and fix while also avoiding the need to harvest large segments of autograft in reconstruction at the diaphysis.[1,25,33] Despite good functional outcomes, intercalary allografts span two bone-graft junctions and are frequently associated with high rates of non-unions.[3,25,34] A study by Ortiz-Cruz et al.[3] reviewed 104 intercalary allograft procedures performed over an 18-year period. They showed that at a mean follow-up of 5.6 years, there was a 92% limb salvage rate, but 31% of those resulted in nonunions necessitating additional procedures. In a review of 135 patients who underwent intercalary allograft reconstruction, Aponte-Tiano et al.[25] showed lower rates of non-union at 17%. Factors affecting risk of non-union in intercalary allografts are related to the use of adjuvant chemotherapy or radiation.[34,35] In the absence of negative prognostic factors such as infection, reoperation after nonunion is not only feasible, but results in regaining of functionality and weight-bearing status.[1,3,25,34] Patients in our study with diaphyseal lesions who

Table 3
Literature review of allograft use and complications experienced.

Author	Year	N	F/U (mo)	Allograft Type	Anatomic Location	Chemo Rate	Infection Rate	Non-Union Rate	Fracture Rate
Gebhardt	1991	53	25	N/A	N/A	N/A	30.19%	22.64%	11.32%
Ortiz-Cruz	1997	104	67.2	Int (100)	N/A	24.04%	12.00%	31.00%	18.00%
Bell	1997	17	48	OA (2), APC (15)	Acetabulum	23.53%	11.76%	5.88%	5.88%
San-Julian	1997	137	> 24	OA (26), Int (46), APC (48)	Multi-Site	N/A	N/A	N/A	10.20%
Probyn	1998	11	45.6	OA (11)	Prox Hum	54.55%	18.18%	0.00%	36.36%
Hornicek	1998	38	N/A	OA (38)	Prox Tib	68.42%	20.00%	11.43%	40.00%
Getty	1999	16	N/A	OA (16)	Prox Hum	31.25%	6.25%	0.00%	25.00%
Donati	2002	22	58	APC (22)	Prox Fem	36.36%	4.55%	4.55%	77.27%
Fox	2002	137	94.8	OA (38), Int (22), APC (69)	Prox Fem	0.00%	10.95%	14.60%	18.98%
Langlais	2003	21	120	APC (21)	Pelvis	33.33%	0.00%	19.05%	19.05%
Hillmann	2003	13	45.5	Massive Allograft	Pelvis	N/A	38.46%	0.00%	7.69%
Mankin	2005	941	N/A	OA (483), Int (282), APC (174)	Multi-Site	42.93%	7.90%	16.15%	18.28%
Huang	2006	19	87.6	n/a	Knee	100.00%	10.53%	5.26%	15.79%
Matejovsky	2006	72	N/A	OA (23), Int (28), APC (1)	Multi-Site	N/A	15.28%	N/A	11.11%
Delloye	2007	24	24	N/A	Pelvis	70.83%	12.50%	12.50%	N/A
Muscolo	2008	22	48	OA (9), Int (13)	Multi-Site	N/A	4.55%	4.55%	13.64%
Ogilve	2009	20	192	OA (20)	N/A	90.00%	10.00%	20.00%	45.00%
Biau	2010	32	N/A	APC (32)	Prox Fem	40.63%	15.63%	9.38%	15.63%
Campanacci	2010	20	124	OA (25)	Knee	100.00%	N/A	N/A	60.00%
Muscolo	2010	52	72	OA (52)	Prox Tib	53.85%	25.00%	N/A	5.77%
Van de Sande	2011	23	120	OA (13), APC (10)	Prox Hum	52.17%	13.04%	8.70%	13.04%
Sha Mo	2013	12	45.7	APC (12)	Knee	41.67%	8.33%	0.00%	8.33%
Angelini	2013	110	13.2	OA (51), APC (59)	Pelvis	N/A	23.64%	N/A	N/A
Rabitsch	2013	5	32	OA (5)	Distal Radius	N/A	0.00%	40.00%	0.00%
Delloye	2014	116	103	OA (42), Int (27), APC (47)	N/A	52.59%	6.03%	38.79%	18.10%
Campanacci	2015	19	78	APC (19)	Prox Tib	52.63%	5.26%	10.53%	31.58%
Aponte-Tinao	2015	135	101	Int (135)	Lower Extremity	63.70%	2.96%	17.04%	14.07%
Farfalli	2015	19	91	OA (19)	Prox Hum	N/A	0.00%	0.00%	15.79%
Aponte-Tinao	2015	673	106	OA (272), Int (246), APC (155)	N/A	41.60%	8.92%	N/A	N/A
Jamshidi	2017	22	81	OA (22)	Distal Fem	100.00%	9.09%	13.64%	9.09%
Albergo	2017	45	94.8	OA (45)	Prox Tib	62.22%	20.00%	0.00%	6.67%
Yao	2017	15	21.66	OA (5), Int (10)	Knee	100.00%	6.67%	53.33%	13.33%
Total		**2965**	**82.4**			**46.68%**	**11.92%**	**13.81%**	**20.17%**

Abbreviations: N (sample size), F/U (follow-up), Mo (months), Chemo (Chemotherapy), OA (osteoarticular allograft), Int (intercalary allograft), APC (allograft prosthetic composite), N/A (data not available), Prox (proximal), Fem (Femur), Tib (Tibia).

underwent reconstruction with intercalary allograft most frequently encountered a complication of nonunion. Despite this, autograft supplementation resulted in 88% allograft preservation and 98% limb salvage. Recent advances in intercalary prosthetic design have expanded the available options for reconstruction following resection.[51–55] However, with the increase in survival for patients with musculoskeletal tumors, concerns regarding the long-term durability of these endoprostheses remain. In appropriately selected patients, intercalary allograft reconstruction remains a viable option.

Osteoarticular allografts allow for preservation of opposing native joint structure at the risk of subchondral fragmentation and degeneration of articular cartilage.[36] Fractures are commonly stated as the most frequent complication after osteoarticular reconstruction, requiring supplemental graft or conversion to endoprosthesis.[5,7,37] Ogilvie et al.[7] retrospectively reviewed 20 patients treated with osteoarticular allografts at a mean follow-up of 16 years. Within their series, 45% experienced fractures of the allograft. Literature has proposed that to avoid high fracture rates, the number of screws should be minimized or intramedullary fixation used to reduce creation of stress risers contributing to fracture risk.[38–41] Even with high fracture rates, the advantage of maintaining native articular cartilage has been noted to be particularly important for younger patients whose physes remain open. In our study, one skeletally immature patient treated with osteoarticular allograft suffered fracture following reaching skeletal maturity and was successfully converted to an endoprosthesis without requirement for limb lengthening procedures. Additionally, only one (7%) patient suffered infection following osteoarticular allograft. The value of retention of native structures at the adjacent joint should make osteoarticular allograft a consideration in reconstruction following

resection of primary disease at the joint surface in young patients.

Allograft prosthetic composites are unique in that they combine the longstanding biological durability of allografts with the immediate mechanical endurance of endoprostheses.[43] The use of skeletal allograft surrounding an endoprosthesis allows for improved distribution of forces, while also providing a biologic surface for reattachment of tendons.[45] Allograft prosthetic composites are difficult and very technically involved, requiring longer operating time and thus potential increased risk of infection. Additionally, studies have widely reported high rates of fracture, often attributed to allograft resorption.[46–48] In a study by Biau et al.,[47] there was a 15.63% occurrence of both infection and fractures in patients treated with allograft prosthetic composites at a median follow-up of 68 months. Similarly, Campanacci et al.[46] reported a 31.5% fracture rate. Regardless of reported rates of complications, allograft prosthetic composites show improved functionality and durability when compared to endoprostheses.[36] We found a 10% fracture rate and 10% infection rate following allograft prosthetic composite reconstruction, with a 95% limb salvage rate following management of complications.

Several factors related to treatment and diagnoses were associated with increased risk of complication in our study. Patients undergoing chemotherapy were greater than four times as likely to experience allograft complications. Hornicek et al.[34] found a 27% rate of nonunion in patients who required chemotherapy compared with a rate of 11% in patients who did not. Ortiz-Cruz et al.[3] found patients treated with chemotherapy or radiation to be associated with a 40% failure rate in allograft reconstruction, compared with a 9% failure rate in those who did not require chemotherapy. Chemotherapy has been proposed to delay new bone production at the allograft-host junction, as this site

contains active replication and differentiation of cells, making it particularly susceptible to chemotherapy.[34] Additionally, radiation and chemotherapy may interfere with wound healing, increasing healing time as well as contributing to soft-tissue failure. Local irradiation often leads to fibrosis and edema of surrounding tissue, resulting in impaired functionality. Furthermore, devascularization of surrounding tissue beds and increased graft or wound necrosis may also occur as the result of chemotherapy.[49]

While patients younger than 30 years had increased rates of complication, concurrent associated factors of longer follow-up and a high proportion of disease requiring chemotherapy may have played a role in these findings. Despite this, it is important to highlight this risk of reoperation in younger patients in the pre-surgical discussion with patients and families. A very long-term study on endoprosthetic replacement by Grimer et al.[50] found that patients required a mean of 2.7 additional procedures in their lifetime and highlighted the risks for failure particularly in younger patients. With overall limb retention rates above 95% in patients with allograft, complications are manageable and comparable in risk of re-operation to endoprostheses, as well as providing the numerous advantages of biologic reconstruction in younger patients.

There are several limitations to this study. First, this study is retrospective in nature and subject to the inherent flaws of retrospective study design. Next, this study spans multiple decades, in which time there have been numerous advances in prosthetic design, contributing to an increased institutional tendency to pursue endoprosthetic reconstruction over allograft. Further, this study attempts to apply a relatively recent allograft failure classification system retrospectively. However, it is the hope of the authors that this method will provide a way to organize failures and treatment options. Patients treated with allograft reconstruction were young and with primary disease. The results of this study are not applicable to patients with metastatic disease.

In conclusion, even with advances in prosthetic design, large segment allografts remain viable options with an overall limb salvage rate of 96%. The use of allograft reconstruction provides joint preservation, allows for more biologic reconstruction, and retains greater bone stock for subsequent revision surgeries. Despite complication rates, subsequent management with an algorithmic approach results in successful outcomes with a high limb retention rate.

References

1. Aponte-Tinao L, et al. Intercalary femur allografts are an acceptable alternative after tumor resection. *Clin Orthop Relat Res.* 2012;470(3):728–734.
2. Gebhardt MC, et al. The use of bone allografts for limb salvage in high-grade extremity osteosarcoma. *Clin Orthop Relat Res.* 1991(270):181–196.
3. Ortiz-Cruz E, et al. The results of transplantation of intercalary allografts after resection of tumors. A long-term follow-up study. *J Bone Joint Surg Am.* 1997;79(1):97–106.
4. Aho AJ, et al. Incorporation and clinical results of large allografts of the extremities and pelvis. *Clin Orthop Relat Res.* 1994(307):200–213.
5. Getty PJ, Peabody TD. Complications and functional outcomes of reconstruction with an osteoarticular allograft after intra-articular resection of the proximal aspect of the humerus. *J Bone Joint Surg Am.* 1999;81(8):1138–1146.
6. Hejna MJ, Gitelis S. Allograft prosthetic composite replacement for bone tumors. *Semin Surg Oncol.* 1997;13(1):18–24.
7. Ogilvie CM, et al. Long-term results for limb salvage with osteoarticular allograft reconstruction. *Clin Orthop Relat Res.* 2009;467(10):2685–2690.
8. Rödl RW, et al. Osteoarticular allograft in surgery for high-grade malignant tumours of bone. *J Bone Joint Surg Br.* 2000;82(7):1006–1010.
9. Muscolo DL, et al. Intercalary femur and tibia segmental allografts provide an acceptable alternative in reconstructing tumor resections. *Clin Orthop Relat Res.* 2004(426):97–102.
10. Thompson RC, et al. Fractures in large-segment allografts. *Clin Orthop Relat Res.* 2000(370):227–235.
11. Thompson RC, Pickvance EA, Garry D. Fractures in large-segment allografts. *J Bone Joint Surg Am.* 1993;75(11):1663–1673.
12. Vander Griend RA. The effect of internal fixation on the healing of large allografts. *J Bone Joint Surg Am.* 1994;76(5):657–663.
13. Delloye C, et al. Bone allografts: what they can offer and what they cannot. *J Bone Joint Surg Br.* 2007;89(5):574–579.
14. Muscolo DL, et al. Unicondylar osteoarticular allografts of the knee. *J Bone Joint Surg Am.* 2007;89(10):2137–2142.
15. Clohisy DR, Mankin HJ. Osteoarticular allografts for reconstruction after resection of a musculoskeletal tumor in the proximal end of the tibia. *J Bone Joint Surg Am.* 1994;76(4):549–554.
16. Muscolo DL, et al. Use of distal femoral osteoarticular allografts in limb salvage surgery. *J Bone Joint Surg Am.* 2005;87(11):2449–2455.
17. DeGroot H, et al. The use of cement in osteoarticular allografts for proximal humeral bone tumors. *Clin Orthop Relat Res.* 2004(427):190–197.
18. Gebhardt MC, Roth YF, Mankin HJ. Osteoarticular allografts for reconstruction in the proximal part of the humerus after excision of a musculoskeletal tumor. *J Bone Joint Surg Am.* 1990;72(3):334–345.
19. Muscolo DL, et al. Proximal tibia osteoarticular allografts in tumor limb salvage surgery. *Clin Orthop Relat Res.* 2010;468(5):1396–1404.
20. Toy PC, et al. Distal femoral osteoarticular allografts: long-term survival, but frequent complications. *Clin Orthop Relat Res.* 2010;468(11):2914–2923.
21. Aponte-Tinao LA, et al. What are the risk factors and management options for infection after reconstruction with massive bone allografts? *Clin Orthop Relat Res.* 2016;474(3):669–673.
22. Gitelis S, et al. The use of large allografts for tumor reconstruction and salvage of the failed total hip arthroplasty. *Clin Orthop Relat Res.* 1988(231):62–70.
23. Gitelis S, Piasecki P. Allograft prosthetic composite arthroplasty for osteosarcoma and other aggressive bone tumors. *Clin Orthop Relat Res.* 1991(270):197–201.
24. Harris AI, et al. Allograft prosthetic composite reconstruction for limb salvage and severe deficiency of bone at the knee or hip. *Semin Arthroplasty.* 1994;5(2):85–94.
25. Aponte-Tinao LA, et al. Should fractures in massive intercalary bone allografts of the lower limb be treated with ORIF or with a new allograft? *Clin Orthop Relat Res.* 2015;473(3):805–811.
26. Dick HM, Strauch RJ. Infection of massive bone allografts. *Clin Orthop Relat Res.* 1994(306):46–53.
27. Lord CF, et al. Infection in bone allografts. Incidence, nature, and treatment. *J Bone Joint Surg Am.* 1988;70(3):369–376.
28. Henderson ER, et al. Classification of failure of limb salvage after reconstructive surgery for bone tumours : a modified system Including biological and expandable reconstructions. *Bone Joint Lett J.* 2014;96-B(11):1436–1440.
29. Enneking WF, et al. A system for the functional evaluation of reconstructive procedures after surgical treatment of tumors of the musculoskeletal system. *Clin Orthop Relat Res.* 1993(286):241–246.
30. Benevenia J, et al. Outcomes of a modular intercalary endoprosthesis as treatment for segmental defects of the femur, tibia, and humerus. *Clin Orthop Relat Res.* 2015;474(2):539–548.
31. Albergo JI, et al. Proximal tibia reconstruction after bone tumor resection: are survivorship and outcomes of endoprosthetic replacement and osteoarticular allograft similar? *Clin Orthop Relat Res.* 2017;475(3):676–682.
32. Brien EW, et al. Allograft reconstruction after proximal tibial resection for bone tumors. An analysis of function and outcome comparing allograft and prosthetic reconstructions. *Clin Orthop Relat Res.* 1994(303):116–127.
33. Farfalli GL, et al. Clinical and functional outcomes of tibial intercalary allografts after tumor resection. *Orthopedics.* 2012;35(3):e391–e396.
34. Hornicek FJ, et al. Factors affecting nonunion of the allograft-host junction. *Clin Orthop Relat Res.* 2001(382):87–98.
35. Mankin HJ, et al. Osteoarticular and intercalary allograft transplantation in the management of malignant tumors of bone. *Cancer.* 1982;50(4):613–630.
36. Gilbert NF, et al. Allograft-prosthetic composite reconstruction of the proximal part of the tibia. An analysis of the early results. *J Bone Joint Surg Am.* 2009;91(7):1646–1656.
37. Probyn LJ, et al. A comparison of outcome of osteoarticular allograft reconstruction and shoulder arthrodesis following resection of primary tumours of the proximal humerus. *Sarcoma.* 1998;2(3-4):163–170.
38. Berrey Jr BH, et al. Fractures of allografts. Frequency, treatment, and end-results. *J Bone Joint Surg Am.* 1990;72(6):825–833.
39. Dion N, Sim FH. The use of allografts in musculoskeletal oncology. *Instr Course Lect.* 2002;51:499–506.
40. Hornicek Jr FJ, et al. Limb salvage with osteoarticular allografts after resection of proximal tibia bone tumors. *Clin Orthop Relat Res.* 1998(352):179–186.
41. Sorger JI, et al. Allograft fractures revisited. *Clin Orthop Relat Res.* 2001(382):66–74.
42. Mankin HJ, et al. Current status of allografting for bone tumors. *Orthopedics.* 1992;15(10):1147–1154.
43. Ogura K, et al. *Intercalary Reconstruction after Wide Resection of Malignant Bone Tumors of the Lower Extremity Using a Composite Graft with a Devitalized Autograft and a Vascularized Fibula.* Sarcoma; 2015:861575 2015.
44. Gautam D, Malhotra R. Megaprosthesis versus allograft prosthesis composite for massive skeletal defects. *J Clin Orthop Trauma.* 2018;9(1):63–80.
45. Muller DA, et al. Allograft-prosthetic composite versus megaprosthesis in the proximal tibia-What works best? *Injury.* 2016;47(Suppl 4):S124–S130.
46. Campanacci L, et al. Resurfaced allograft-prosthetic composite for proximal tibial reconstruction in children: intermediate-term results of an original technique. *J Bone Joint Surg Am.* 2015;97(3):241–250.
47. Biau DJ, et al. Results of 32 allograft-prosthesis composite reconstructions of the proximal femur. *Clin Orthop Relat Res.* 2010;468(3):834–845.
48. Langlais F, et al. Long-term results of allograft composite total hip prostheses for tumors. *Clin Orthop Relat Res.* 2003(414):197–211.
49. Sharma DN, et al. Perioperative high-dose-rate interstitial brachytherapy combined with external beam radiation therapy for soft tissue sarcoma. *Brachytherapy.* 2015;14(4):571–577.
50. Grimer RJ, et al. Very long-term outcomes after endoprosthetic replacement for malignant tumours of bone. *Bone Joint Lett J.* 2016;98-B(6):857–864.
51. Ahlmann ER, Menendez LR. Intercalary endoprosthetic reconstruction for diaphyseal

bone tumours. *J Bone Joint Surg Br.* 2006;88(11):1487–1491.

52. Aldlyami E, et al. Endoprosthetic replacement of diaphyseal bone defects. Long-term results. *Int Orthop.* 2005;29(1):25–29.

53. Benevenia J, et al. Outcomes of a modular intercalary endoprosthesis as treatment for segmental defects of the femur, tibia, and humerus. *Clin Orthop Relat Res.*

2016;474(2):539–548.

54. Gibson PD, Ippolito JA, Benevenia J. Radial shaft reconstruction with an intercalary endoprosthesis following resection of metastatic tumor. *Orthopedics.* 2016:1–6.

55. Sewell MD, et al. Intercalary diaphyseal endoprosthetic reconstruction for malignant tibial bone tumours. *J Bone Joint Surg Br.* 2011;93(8):1111–1117.