Before the appearance of therapeutic chemotherapy and radiotherapy, malignant tumors of the extremities were usually treated with radical amputation. The majority of bone sarcomas occur about the hip and knee joints; therefore, patients were frequently treated with hip disarticulation or above-knee amputation.\[1–3\]

However, the survival rate after amputation was consistently poor, especially for the pediatric population. In Price et al.\[4\] study in 1975, the five-year disease-free survival rate after early amputation was 12%. Similarly, Campanacci and Cervellati\[5\] reported an overall ten-year survival rate of 5% after radical amputation in patients with osteosarcoma with no survival of children under fifteen years. After the development of chemotherapy, the five-year survival rates promptly improved to 50%-65%.\[6–9\]

This improved capability to control the disease process allowed the orthopedic oncologists to attempt limb salvage, instead of amputation, as a part of multimodal therapy for malignant tumors of limbs, especially in pediatric patients with no difference in patient survival following limb-salvage surgery as compared with amputation. Improvements in biological reconstructive methods, as well as endoprosthetic design, allow effective limb-salvage choices after oncological resections in pediatrics that are ideally adjusted to the patient’s unique functional needs.

Keywords: Ewing’s sarcoma, limb salvage, malignant limb tumors, pediatrics, team approach, osteosarcoma
Challenges and limb salvage has been less enthusiastically affirmed for pediatrics as compared with adults.[16–18] This discrepancy is because children can more easily adapt to amputation than adults with a reliable outcome after amputation compared to limb-salvage that has a high probability of complications which often require further surgical interventions.[16,17] Moreover, surgical reconstructions in pediatrics are challenging with the fact that a physis is usually sacrificed resulting in a clinically significant leg-length discrepancy.[18–20] These factors are critical in choosing the appropriate surgical procedure. Consequently, expandable prostheses have been developed as a solution to limb length inequality after sacrificing the physis with acceptable results.[21–24]

Osteosarcoma is the most common primary bone sarcoma and it preferentially affects children in the second decade of life, with the majority of cases affecting the distal part of the femur and proximal part of the tibia.[25,26] Ewing sarcoma also affects adolescents and represents approximately 10 to 15% of malignant bone tumors.[27,28]

The purpose of this review article is to highlight the multidisciplinary team approach for limb salvage for malignant bone tumors of the limb in the pediatric patients, and review the current options for limb-salvage, with key elements of the decision-making process.

**Clinical Scenario**

A 16-year-old previously healthy male who presented to our orthopedic outpatient clinic, accompanied by his father, with right arm pain. He reported that pain started 6 weeks prior to presentation and it was initially noted on activity, with occasional night pain which was somewhat relieved by rest and analgesics.

Clinical examination revealed mild swelling and tenderness over the right arm with slight limitation of the right shoulder as compared to the left shoulder. Vital signs were within the normal ranges.

Plain radiographs demonstrated a well-defined periosteal reaction and sclerotic lesion over the mid-shaft of the right humerus, Figure 1.

Axial and sagittal computed tomographic (CT) images of the humerus better depicted the aggressive periosteal reaction and the bone marrow involvement.

Magnetic resonance imaging (MRI) demonstrated the diaphyseal lesion centered in the marrow canal of the humerus with circumferential soft-tissue extension. The lesion was heterogeneously intermediate in signal intensity on both the T1-weighted and T2-weighted images, Figure 2.

Metastatic tumor workup was done and the whole-body bone scintigraphy showed markedly increased uptake of radionuclide in the humeral lesion with no abnormalities in other parts of the body. Chest CT scan and laboratory investigations showed no abnormalities.

Open biopsy was performed and it demonstrated features of Ewing’s sarcoma. The patient was then sent to the pediatric oncologist and he received 3 cycles of chemotherapy preoperatively.

Surgical resection of the 14 cm of the humerus was done with intercalary fibular autograft of 18 cm. Fixation was achieved using proximal humeral locked plate and screws, Figures 3, 4. Specimen was sent for histopathological examination and the report confirmed the diagnosis of Ewing’s sarcoma. The patient was then sent for neoadjuvant chemotherapy and radiotherapy.
Multidisciplinary Approach

A multidisciplinary approach is required for limb salvage surgery in pediatrics with malignant bone tumors such as osteosarcoma and Ewing’s sarcoma.[29] The surgery should be done in highly specialized centers which are able to provide a full spectrum of care and where the multidisciplinary team of orthopedic surgeon, oncologist, histopathologist, radiologist, and radiotherapist can interact and cooperate.[29,30]

1) Orthopedic Oncologist: Initial Evaluation

The initial visit with the orthopedic oncologist sets the plan for evaluation and treatment which the patient will undergo in the following weeks, so it is crucial to develop a trustful relationship with the child and the family.[19,31] In bone tumors, initial evaluation requires a full understanding of the clinical presentation, symptom duration, and severity.[18]

A thorough history and physical examination with characteristic findings on standard radiographs often enable the orthopedic oncologist to make a potential diagnosis.[18,29]

2) Radiologist: Diagnostic Imaging

The radiologist has a crucial role in assessing the character and extent of local tumor and the presence of regional or distant metastases.[32,33] Radiographically, the appearance of malignant bone tumors may be osteolytic, osteoblastic,
or mixed.\[34\] Furthermore, radiographs may show cortical destruction and periosteal elevation with soft tissue masses in most cases.\[35,36\]

Magnetic resonance imaging (MRI) is considered the best radiological modality to evaluate the intramedullary extension and the association with the nearby muscles, vessels, nerves, and soft tissues.\[37\]

3) Orthopedic Oncologist: Obtaining a Biopsy

The final and crucial step toward definitive diagnosis is obtaining a biopsy which may be an open or a large core tissue biopsy.\[38\]

Fine-needle aspiration biopsy should be avoided as it often results in under- or incorrect diagnosis. The biopsy tract should ideally be set in an area that can be totally excised in the definitive surgery.\[39,40\]

4) Pathologist: Tissue Diagnosis

The pathologist is involved in the diagnosis of tumors at the point of biopsy to confirm the diagnosis assumed on clinical and radiological evaluation, and also at the time of the resection to evaluate the status of the surgical margins and estimate the response to neoadjuvant chemotherapy.\[40,41\] The pathologist's evaluation helps establish a prognosis and guides in the consequent clinical care.\[41,42\]

5) Pediatric Oncologist: Neoadjuvant Therapy

Both osteosarcoma and Ewing sarcoma needs the combination of adequate systemic therapy in addition to the local control of all macroscopic tumors.\[43\]

Rosen et al.\[44\] was the first to introduce the use of neoadjuvant chemotherapy before the definitive management and proposed that this concept would have a potential role in facilitating limb-salvage procedures.

Neoadjuvant and adjuvant chemotherapy have a significant role in patients with malignant bone tumors, even in those with localized disease due to the presence of micrometastases not visible even with modern techniques.\[45\] Osteosarcomas are relatively radioresistant, therefore radiotherapy is not effective.\[44,45\]

Currently, the most used chemotherapy agents include cisplatin, doxorubicin, ifosfamide, and methotrexate.\[25,28\]

6) Orthopedic Oncologist: Preoperative Planning and Definitive Surgical Management

Following neoadjuvant chemotherapy and repeated imaging, the orthopedic oncologist should meet with the patient and the family for pre-operative evaluation and discussion of the possible surgical management and limb reconstruction options and the expected postoperative management.\[8,46\] Besides the social concerns, preoperative planning include also technical considerations of surgery.\[26,29\]

Limb-Salvage Surgical Options

The surgical management of limb sarcomas is performed in two steps; tumor excision and limb reconstruction.\[13\] Complete tumor resection must be performed and reconstructive concerns should not interfere with obtaining an adequate margin of resection.\[47\] However, some sites, such as the proximal part of the fibula, may not need reconstruction of any structures except the lateral collateral ligament.\[44,49\]

Reconstructive techniques include biological, endoprosthetic reconstructions, and rotationplasty.\[50\] Biological reconstruction options involve the use of autografts such as vascularized or nonvascularized fibula, allograft, combined autograft-allograft, and bone transport.\[51\] The main benefit of biological reconstructions is the probability of a satisfactory resolution.\[51,52\] For malignant neoplasms sparing the joint, intercalary biological reconstructions can almost always be done. The main drawback is that the constructs frequently demand prolonged duration of immobilization and limited weight-bearing.\[52,53\]

For endoprosthetic reconstructions, various metallic endoprosthetic choices and customization that permits several adjustments, including the extension capacity, are available. The main benefits of megaprostheses are their strength and durability, allowing immediate postoperative weight-bearing.\[54\] The main drawback is the inevitable implant failure, such as breakage, wear bearings and fixation problems, that happens over time in patients who have been cured of disease.\[46,54,55\]

The surrounding soft tissues available for coverage may have a fundamental impact on the treatment choices.\[56\] Local rotation flaps may be sufficient, and free tissue transfers may be required in some cases. Free flaps may be soft-tissue grafts only or osteo-fasciocutaneous grafts to cover soft-tissue and skin defects.\[57,58\]

Biological Reconstruction Options

1) Osteoarticular Allograft

For tumors that cross the physis, biological reconstructions may be achieved by osteoarticular allografts. Despite their fixed length, osteoarticular grafts have inherent advantages, including the preservation of the ipsilateral physis on the other side of the joint.\[59,60\]

An osteoarticular allograft is selected based on articular congruity, matching the size of the graft to that of the remaining tibia or femur. Precise matching of the size and shape of the graft than is preferred to be determined by
three-dimensional computer modeling more than the traditional measurements alone.\textsuperscript{[46,52,61]}

2) Transepiphyseal Resection and Reconstruction

Transepiphyseal tumor resection and reconstruction may be done for tumors that do not cross the physis. This approach aims to preserve the viable femoral or tibial articular surface and the ligamentous structures around the knee.\textsuperscript{[62]} This approach may require sacrificing the physis to obtain adequate resection margins, so additional procedures for addressing limb-length inequality may be necessary.

Ideally, at least 1 cm of bone should be preserved after resection.\textsuperscript{[63]} Contoured locking plates allow for large locking screws to be used to fix into the remaining epiphysis.\textsuperscript{[64,65]}

Canadell et al.\textsuperscript{[66]} reported a transphyseal approach for the management of metaphyseal malignant tumors that would require resection of the joint surface. An external fixator was applied with two pins in the epiphysis and another two pins in the diaphysis, around 10 cm away from the tumor.\textsuperscript{[66]} Physeal distraction was begun during neoadjuvant chemotherapy until 2 cm lengthening of the physis. Transepiphyseal resection of the tumor was then performed, and the bone defect was reconstructed with autograft or allograft.\textsuperscript{[66]}

3) Intercalary Resection and Capanna Technique:

Ideally, adequate tumor resection margins could be achieved while preserving the physisal plate, and intercalary resection and reconstruction can be attempted.\textsuperscript{[87]} Significant intercalary bone defects after tumor resections have historically been reconstructed with massive cadaveric allograft, which is associated with multiple complications, including infection, fracture, and nonunion.\textsuperscript{[68,69]}

The Capanna technique for limb reconstruction combines the use of the cadaveric allograft with an intramedullary vascularized fibular graft to allow for immediate rigid fixation of the allograft, and also the fibular graft can hypertrophy with viable bone over time, promoting union rates and reducing late-fracture rates.\textsuperscript{[70,71]}

4) Distraction Osteogenesis and Bone Transport

Bone transport is a procedure that is often used for reconstruction of the bone defects resulting from trauma or infection. At some institutions, this technique is used for reconstruction after tumor resection.\textsuperscript{[72,73]} This technique is less risky and is associated with fewer postoperative risks and more favorable long-term outcomes.\textsuperscript{[74]}

Xu et al.\textsuperscript{[75]} reported full bone healing without any complications or limb discrepancy following treating a 11-year-old male with proximal tibial osteosarcoma with marginal excision with preservation of the proximal epiphysis and metaphyseal reconstruction using distraction osteogenesis.

Similarly, He et al.\textsuperscript{[76]} reported satisfactory results with no local recurrence or metastasis after treating 7-year-old male with distal tibial osteosarcoma with physeal distraction, en-bloc resection, and distraction osteogenesis.

Endoprosthetic Reconstruction

There are numerous endoprosthetic options for limb-salvage surgery in pediatrics. Modular prostheses allow for most reconstructions for the proximal or distal parts of the femur or even the whole femur.\textsuperscript{[47]} Proximal tibial reconstructions support insertion sites for the patellar tendon and hamstring muscles.\textsuperscript{[77]} For pediatrics, the two major concerns are a stem-fixation option and the ability of longitudinal extension.\textsuperscript{[78]}

There are variable stem-fixation options including cemented, press-fit, and compressive osseointegration implants, which are surgeon preference. Cemented and press-fit stems have varying lengths and diameters.\textsuperscript{[79]} Custom stems may be needed in young pediatrics with small medullary canal. The advantage of cemented stems is that they provide immediate stability and weight-bearing capability, unlike press-fit stems which may need delayed weight bearing.\textsuperscript{[79-81]}

Highly polished stems can be used on the other side of the joint that is being resurfaced to accommodate the megaprosthes.\textsuperscript{[82]} Only the articular surface should be cut with preservation of the physis to allow growth around the stem. Even with careful attention to technique and implant choice, these reconstructions present a substantial risk for proximal tibial growth disturbance.\textsuperscript{[55,82]} Trialing of the desired reconstruction combination is crucial to guarantee ideal limb length, alignment, rotation, and patellar tracking.\textsuperscript{[83,84]}

Extendable Megaprostheses

Extendable or expandable megaprostheses have gained enormous popularity as they have the ability of longitudinal extension with a tube within a tube design which lengthens like a telescope offering a great alternative to amputation in growing pediatrics. However, early failure and high revision rates are the primary concerns.\textsuperscript{[21,48,85,86]}

The extension mechanisms include invasive and noninvasive methods. The invasive mechanisms, which require open surgical procedure, include worm-gear and segmental block-expansion mechanisms.\textsuperscript{[87]} The worm-gear mechanism uses a screwdriver equivalent to rotate the gear and lengthen the implant. The segmental block-expansion de-
vice involves a metallic segment to be inserted along the diaphysis of the component after distraction.\textsuperscript{[55,82,87]}

Noninvasive designs avoid surgical incisions and use an external electric coil to produce a rotating magnetic field through a magnet placed inside the implant to drive the gear device, with a lengthening rate of 1 mm per 4 minutes.\textsuperscript{[88,89]}

Reported complications following reconstruction by extendable prostheses included infection, aseptic loosening, failure of the extension apparatus, and fracture around the implants.\textsuperscript{[85,89–92]}

Rotationplasty

One of the options for limb salvage in immature patients with malignant tumors around the knee is rotationplasty, which was developed as an alternative to above-knee amputation. Rotationplasty converts the ankle to work as a knee joint with foot preservation so that patients do not feel that they are amputees. This new knee has active flexion of nearly 90° and has a short rehabilitation period with a prosthesis with more dynamic and efficient gait.\textsuperscript{[93]} Rotationplasty has reported satisfactory outcomes and acceptable cosmetic appearance.\textsuperscript{[93,94]}

Conclusion

Limb salvage of a malignant lesion during childhood is a multidisciplinary team approach which necessitates collaboration of many specialties (orthopedic oncologist, pediatric oncologist, radiologist, pathologist, radiotherapist, physiotherapist, and psychotherapist) and it carries a major challenge. The decision to proceed with limb salvage is often more difficult than many patients and families. Initially, realize. For the growing child, several options exist for limb salvage after resection of extremity bone sarcoma, including biological and endoprosthetic reconstructions, although current data do not support one clear choice. Careful planning and thoughtful guidance are needed for such patients because the many patient and tumor-specific factors often dictate the long-term oncological and functional success of the procedure.

Disclosures

Ethics Committee Approval: The Ethics Committee of Menoufa University Hospital provided the ethics committee approval for this study (10.01.2019-MNF-19-2570).

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References

1. Cortes EP, Holland JF, Wang JJ, Sinks LF, Blom J, Senn H, et al. Amputation and adriamycin in primary osteosarcoma. N Engl J Med 1974;291:998–1000. [CrossRef]
2. Woodruff M. The challenge of osteosarcoma. Ann R Coll Surg Engl 1969;44:299–307.
3. Campanacci M, Laus M. Local recurrence after amputation for osteosarcoma. J Bone Joint Surg Br 1980;62-b:201–7. [CrossRef]
4. Price CH, Zhuber K, Salzer-Kuntschik M, Salzer M, Willert HG, Immenkamp M, et al. Osteosarcoma in children. A study of 125 cases. J Bone Joint Surg Br 1975;57:341–5. [CrossRef]
5. Campanacci M, Cervellati G. Osteosarcoma: A review of 345 cases. Ital J Orthop Traumatol 1975;1:5–22.
6. Sinks LF, Mindell ER. Chemotherapy of osteosarcoma. Clin Orthop Relat Res 1975:101–4. [CrossRef]
7. Jaffe N. The potential for an improved prognosis with chemotherapy in osteogenic sarcoma. Clin Orthop Relat Res 1975:111–8. [CrossRef]
8. van Oosterwijk JG, Anninga JK, Gelderblom H, Cleton-Jansen AM, Bovee JV. Update on targets and novel treatment options for high-grade osteosarcoma and chondrosarcoma. Hematol Oncol Clin North Am 2013;27:1021–48. [CrossRef]
9. Cohen JJ, Kaplinsky C, Katz K, Mor C, Goshen Y, Yaniv Y, et al. Improved results in osteogenic sarcoma 1973–79 vs. 1980–86: analysis of results from a single center. Isr J Med Sci 1993;29:27–9.
10. Simon MA, Aschliman MA, Thomas N, Mankin HJ. Limb-salvage treatment versus amputation for osteosarcoma of the distal end of the femur. J Bone Joint Surg Am 1986;68:1331–7.
11. Eilber FR, Mirra JJ, Grant TT, Weisenburger T, Morton DL. Is amputation necessary for sarcomas? A seven-year experience with limb salvage. Ann Surg 1980;192:431–8. [CrossRef]
12. 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;76:649–56. [CrossRef]
13. Choong PF, Sim FH. Limb-sparing surgery for bone tumors: new developments. Semin Surg Oncol 1997;13:64–9. [CrossRef]
14. Carty CP, Bennett MB, Dickinson IC, Steadman P. Assessment of kinematic and kinetic patterns following limb salvage procedures for bone sarcoma. Gait Posture 2009;30:547–51.
15. DiCaprio MR, Friedlaender GE. Malignant bone tumors: limb sparing versus amputation. J Am Acad Orthop Surg 2003;11:25–37. [CrossRef]
16. Zahltten-Hinguranage A, Bernd L, Ewerbeck V, Sabo D. Equal quality of life after limb-sparing or ablative surgery for lower extremity sarcomas. Br J Cancer 2004;91:1012–4. [CrossRef]
17. Ottaviani G, Robert RS, Huh WW, Palla S, Jaffe N. Sociooccupational and physical outcomes more than 20 years after the
diagnosis of osteosarcoma in children and adolescents: limb salvage versus amputation. Cancer 2013;119:3727–36.

18. Worch J, Matthay KK, Neuhaus J, Goldsby R, DuBois SG. Osteosarcoma in children 5 years of age or younger at initial diagnosis. Pediatr Blood Cancer 2010;55:285–9. [CrossRef]

19. Varan A, Yazici N, Aksoy C, Gedikoglu G, Yalcin B, Akyuz C, et al. Treatment results of pediatric osteosarcoma: twenty-year experience. J Pediatr Orthop 2007;27:241–6.

20. Hudson MM, Tyc VL, Cremer LK, Luo X, Li H, Rao BN, et al. Patient satisfaction after limb-sparing surgery and amputation for pediatric malignant bone tumors. J Pediatr Oncol Nurs 1998;15:60–9; discussion 70–1. [CrossRef]

21. Henderson ER, Pepper AM, Marulanda G, Binetie OT, Cheong D, Letson GD. Outcome of lower-limb preservation with an expandable endoprosthetic after bone tumor resection in children. J Bone Joint Surg Am 2012;94:537–47. [CrossRef]

22. Dominkus M, Krepler P, Schwameis E, Windhager R, Krotz R. Growth prediction in extendable tumor prostheses in children. Clin Orthop Relat Res 2001:212–20. [CrossRef]

23. Meswania JM, Taylor SJ, Blunn GW. Design and characterization of a novel permanent magnet synchronous motor used in a growing prosthesis for young patients with bone cancer. Proc Inst Mech Eng H 2008;222:393–402. [CrossRef]

24. Gitelis S, Neel MD, Wilkins RM, Rao BN, Kelly CM, Yao TK. The use of a closed expandable prosthesis for pediatric sarcomas. Chir Organi Mov 2003:88:327–33.

25. Isakoff MS, Bielack SS, Meltzer P, Gorlick R. Osteosarcoma: Current and future therapeutic approaches for osteosarcoma. Expert Rev Anticancer Ther 2018;18:39–50. [CrossRef]

26. Harrison DJ, Geller DS, Gill JD, Lewis VO, Gorlick R. Current and future therapeutic approaches for osteosarcoma. Expert Rev Anticancer Ther 2018;18:39–50. [CrossRef]

27. Krides WB, Toumi N, Chaari H, Khanfir A, Ayaki K, Keskes H, et al. A Review of Ewing Sarcoma Treatment: Is it Still a Subject of Debate? Rev Recent Clin Trials 2017;12:19–23. [CrossRef]

28. Gaspar N, Hawkins DS, Dirksen U, Lewis VO, Ferrari S, Le Deley MC, et al. Ewing Sarcoma: Current Management and Future Approaches Through Collaboration. J Clin Oncol 2015;33:3029–35. [CrossRef]

29. Wittig JC, Bickels J, Priebat D, Jelinek J, Kellar-Graney K, Shmoooker B, et al. Osteosarcoma: a multidisciplinary approach to diagnosis and treatment. Am Fam Physician 2002;65:1123–32.

30. Biazzo A, De Paolis M. Multidisciplinary approach to osteosarcoma. Acta Orthop Belg 2016;82:690–8. [CrossRef]

31. Arndt CA, Crist WM. Common musculoskeletal tumors of childhood and adolescence. N Engl J Med 1999;341:342–52.

32. Lewis VO, Morris CD, Parsons TW, 3rd. Malignant and benign bone tumors that you are likely to see. Instr Course Lect 2013;62:535–49.

33. Claye M. Many faces of osteosarcoma on plain radiographs. ANZ J Surg 2015;85:22–6. [CrossRef]

34. Rosenberg ZS, Lev S, Schmahmann S, Steiner GC, Beltran J. Present D. Osteosarcoma: subtle, rare, and misleading plain film features. AJR Am J Roentgenol 1995;165:1209–14. [CrossRef]

35. Spina V, Montanari N, Romagnoli R. Malignant tumors of the osteogenic matrix. Eur J Radiol 1998;27 Suppl 1:S98–109.

36. Simpson E, Brown HL. Understanding osteosarcomas. Jaapa 2018;31:15–9. [CrossRef]

37. Saifuddin A, Sharif B, Gerrand C, Whelan J. The current status of MRI in the pre-operative assessment of intramedullary conventional appendicular osteosarcoma. Skeletal Radiol 2019;48:503–16. [CrossRef]

38. Picci P. Osteosarcoma (osteogenic sarcoma). Orphanet J Rare Dis 2007;2.6. [CrossRef]

39. Panzica M, Luke U, Mommsen P, Krettek C. [Biopsy and approach routes for bone tumors. Where and how much is sufficient?]. Unfallchirurg 2014;117:501–9. [CrossRef]

40. Gambarotti M, Dei Tos AP, Vanel D, Picci P, Gibertoni D, Klein MJ, et al. Osteoblastoma-like osteosarcoma: high-grade or low-grade osteosarcoma? Histopathology 2019;74:494–503.

41. Puls F, Niblett AJ, Mangham DC. Molecular pathology of bone tumours: diagnostic implications. Histopathology 2014;64:461–76. [CrossRef]

42. Hayashi K, Tsuchiya H, Yamamoto N, Shirai T, Nishida H, Takeuchi A, et al. Diagnosis and treatment of low-grade osteosarcoma: experience with nine cases. Int J Clin Oncol 2014;19:731–8. [CrossRef]

43. Meyers PA. Systemic therapy for osteosarcoma and Ewing sarcoma. Am Soc Clin Oncol Educ Book 2015:e644–7. [CrossRef]

44. Rosen G, Murphy ML, Huvos AG, Gutierrez M, Marcove RC. Chemotherapy, en bloc resection, and prosthetic bone replacement in the treatment of osteogenic sarcoma. Cancer 1976;37:1–11. [CrossRef]

45. Jimmy R, Stern C, Lisy K, White S. Effectiveness of mifamurtide in addition to standard chemotherapy for high-grade osteosarcoma: a systematic review. JBI Database System Rev Implement Rep 2017;15:2113–52. [CrossRef]

46. Yang Y, Han L, He Z, Li X, Yang S, Yang J, et al. Advances in limb salvage treatment of osteosarcoma. J Bone Oncol 2018;10:36–40. [CrossRef]

47. Ma ZT, Li HG. Limb-salvage for osteosarcoma. Chin Med J (Engl) 1994;107:854–7. [CrossRef]

48. Grimer RJ, Aydin BK, Wafa H, Carter SR, Jeys L, Abudu A, et al. Very long-term outcomes after endoprosthetic replacement for malignant tumours of bone. Bone Joint J 2016;98-B:857–64. [CrossRef]

49. Myers GJ, Abudu AT, Carter SR, Tillman RM, Grimer RJ. Endoprosthetic replacement of the distal femur for bone tumours: long-term results. J Bone Joint Surg Br 2007;89:521–6. [CrossRef]

50. Funovics PT, Bucher F, Toma CD, Kotz RI, Dominkus M. Treatment and outcome of parosteal osteosarcoma: bio-
logical versus endoprosthetic reconstruction. J Surg Oncol 2011;103:782–9. [CrossRef]
51. San-Julian M, Vazquez-Garcia B. Biological Reconstruction in Bone Sarcomas: Lessons from Three Decades of Experience. Orthop Surg 2016;8:111–21. [CrossRef]
52. Bielack SS, Hecker-Nolting S, Blattmann C, Kager L. Advances in the management of osteosarcoma. F1000Res 2016;5:2767.
53. Campanacci DA, Puccini S, Caff G, Beltrami G, Piccoli A, Innocenti M, et al. Vascularised fibular grafts as a salvage procedure in failed intercalary reconstructions after bone tumour resection of the femur. Injury 2014;45:399–404. [CrossRef]
54. Zhang C, Hu J, Zhu K, Cai T, Ma X. Survival, complications and functional outcomes of cemented megaprostheses for high-grade osteosarcoma around the knee. Int Orthop 2018;42:927–38. [CrossRef]
55. Kamal AF, Rubiansyah P. Clinical outcome of various limb salvage surgeries in osteosarcoma around knee: Megaprostheses, extracorporal irradiation and resection arthrodesis. Ann Med Surg (Lond) 2019;42:14–8. [CrossRef]
56. Muramatsu K, Ihara K, Hashimoto T, Seto S, Taguchi T. Combined use of free vascularised bone graft and extracorporal-ly-irradiated autograft for the reconstruction of massive bone defects after resection of malignant tumour. J Plast Reconstr Aesthet Surg 2007;60:1013–8. [CrossRef]
57. Estrella EP, Wang EH. A Comparison of Vascularized Free Fibular Flaps and Nonvascularized Fibular Grafts for Reconstruction of Long Bone Defects after Tumor Resection. J Reconstr Microsurg 2017;33:194–205. [CrossRef]
58. Bus MP, van de Sande MA, Taminiau AH, Dijkstra PD. Is there still a role for osteoarticular allograft reconstruction in musculoskeletal tumour surgery? a long-term follow-up study of 38 patients and systematic review of the literature. Bone Joint J 2017;99-B:522–30. [CrossRef]
59. Wilson RJ, Sulieman LM, VanHouten JP, Halpern JL, Schwartz HS, Devin CJ, et al. Cost-utility of osteoarticular allograft versus endoprosthetic reconstruction for primary bone sarcoma of the knee: A markov analysis. J Surg Oncol 2017;115:257–65.
60. Fu J, Guo Z, Wang Z, Li X, Fan H, Li J, et al. [Use of four kinds of three-dimensional printing guide plate in bone tumor resection and reconstruction operation]. Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi 2014;28:304–8.
61. Muscolo DL, Ayerza MA, Aponte-Tinao LA, Ranalettea M. Partial epiphyseal preservation and intercalary allograft reconstruction in high-grade metaphyseal osteosarcoma of the knee. J Bone Joint Surg Am 2005;87 Suppl 1(PT 2):226–36. [CrossRef]
62. Weitao Y, Qiqing C, Songtao G, Jiaqiang W. Epiphysis preserving operations for the treatment of lower limb malignant bone tumors. Eur J Surg Oncol 2012;38:1165–70. [CrossRef]
63. Buecker PJ, Berenstein M, Gebhardt MC, Hornicek FJ, Mankin HJ. Locking versus standard plates for allograft fixation after tumor resection in children and adolescents. J Pediatr Orthop 2006;26:680–5. [CrossRef]
64. Mei J, Ni M, Jia GY, Chen YX, Zhu XZ. Intermittent internal fixation with a locking plate to preserve epiphyseal growth function during limb-salvage surgery in a child with osteosarcoma of the distal femur: a case report. Medicine (Baltimore) 2015;94:e830. [CrossRef]
65. Canadell J, Forriol F, Cara JA. Removal of metaphyseal bone tumours with preservation of the epiphysis. Physial distaction before excision. J Bone Joint Surg Br 1994;76:127–32.
66. Panagopoulos GN, Mavrogenis AF, Mauffrey C, Lesensky J, Angelini A, Megaloikonomos PD, et al. Intercalary reconstructions after bone tumor resections: a review of treatments. Eur J Orthop Surg Traumatol 2017;27:737–46. [CrossRef]
67. Betz M, Dumont CE, Fuchs B, Exner GU. Physial distaction for joint preservation in malignant metaphyseal bone tumors in children. Clin Orthop Relat Res 2012;470:1749–54. [CrossRef]
68. Yang Z, Tao H, Ye Z, Jin L, Lin N, Yang D. Bone transport for reconstruction of large bone defects after tibial tumor resection: a report of five cases. J Int Med Res 2018;46:3219–25.
69. Watanabe K, Tsuchiya H, Yamamoto N, Shirai T, Nishida H, Hayashi K, et al. Over 10-year follow-up of functional outcome in patients with bone tumors reconstructed using distraction osteogenesis. J Orthop Sci 2013;18:101–9. [CrossRef]
70. Xu SF, Yu XC, Xu M, Chen X. Successful management of a childhood osteosarcoma with epiphysiolysis and distraction osteogenesis. Curr Oncol 2014;21:e658–62. [CrossRef]
71. He X, Zhang HL, Hu YC. Limb Salvage by Distraction Osteogenesis for Distal Tibial Osteosarcoma in a Young Child: A Case Report. Orthop Surg 2016;8:253–6. [CrossRef]
72. Zhang Y, Yang Z, Li X, Chen Y, Zhang S, Du M, et al. Custom prosthetic reconstruction for proximal tibial osteosarco-
ma with proximal tibiofibular joint involved. Surg Oncol 2008;17:87–95. [CrossRef]

78. Batta V, Coathup MJ, Parratt MT, Pollock RC, Aston WJ, Cannon SR, et al. Uncemented, custom-made, hydroxyapatite-coated collared distal femoral endoprostheses: up to 18 years’ follow-up. Bone Joint J 2014;96-B:263–9. [CrossRef]

79. Schwartz AJ, Kobo JM, Eilber FC, Eilber FR, Eckardt JJ. Cemented distal femoral endoprostheses for musculoskeletal tumor: improved survival of modular versus custom implants. Clin Orthop Relat Res 2010;468:2198–210. [CrossRef]

80. Neel MD, Heck R, Britton L, Daw N, Rao BN. Use of a smooth press-fit stem preserves physeal growth after tumor resection. Clin Orthop Relat Res 2004;125–8. [CrossRef]

81. Li Y, Sun Y, Shan HC, Niu XH. Comparative Analysis of Early Follow-up of Biologic Fixation and Cemented Stem Fixation for Femoral Tumor Prosthesis. Orthop Surg 2019;11:451–9.

82. Ilyas I, Pant R, Kurar A, Moreau PG, Younge DA. Modular megaprosthesis for proximal femoral tumors. Int Orthop 2002;26:170–3. [CrossRef]

83. Natarajan MV, Balasubramanian N, Jayasankar V, Sameer M. Endoprosthetic reconstruction using total femoral custom mega prosthesis in malignant bone tumours. Int Orthop 2009;33:1359–63. [CrossRef]

84. Natarajan MV, Sivaseelam A, Ayyappan S, Bose JC, Sampath Kumar M. Distal femoral tumours treated by resection and custom mega-prosthetic replacement. Int Orthop 2005;29:309–13.

85. Ruggieri P, Mavrogenis AF, Pala E, Romantini M, Manfrini M, Mercuri M. Outcome of expandable prostheses in children. J Pediatr Orthop 2013;33:244–53. [CrossRef]

86. Grimer RJ, Belthour M, Carter SR, Tillman RM, Cool P. Extendible replacements of the proximal tibia for bone tumours. J Bone Joint Surg Br 2000;82:255–60. [CrossRef]

87. Morris CD, Wustrack RL, Levin AS. Limb-Salvage Options in Growing Children with Malignant Bone Tumors of the Lower Extremity: A Critical Analysis Review. JBJS Rev 2017;5:e7.

88. Saghieh S, Abboud MR, Muwakkit SA, Saab R, Rao B, Haidar R. Seven-year experience of using Repiphysis expandable prosthesis in children with bone tumors. Pediatr Blood Cancer 2010;55:457–63. [CrossRef]

89. Picardo NE, Blunn GW, Shekkeris AS, Meswania J, Aston WJ, Pollock RC, et al. The medium-term results of the Stanmore non-invasive extendible endoprosthesis in the treatment of paediatric bone tumours. J Bone Joint Surg Br 2012;94:425–30. [CrossRef]

90. Cipriano CA, Gruzinova IS, Frank RM, Gitelis S, Virkus WW. Frequent complications and severe bone loss associated with the repiphysis expandable distal femoral prosthesis. Clin Orthop Relat Res 2015;473:831–8. [CrossRef]

91. Staals EL, Colangeli M, Ali N, Casanova JM, Donati DM, Manfrini M. Are Complications Associated With the Repiphysis(R) Expandable Distal Femoral Prosthesis Acceptable for Its Continued Use? Clin Orthop Relat Res 2015;473:3003–13. [CrossRef]

92. Dotan A, Dadia S, Bickels J, Nirkin A, Flusser G, Issakov J, et al. Expandable endoprosthesis for limb-sparing surgery in children: long-term results. J Child Orthop 2010;4:391–400.

93. Merkel KD, Gebhardt M, Springfield DS. Rotationplasty as a reconstructive operation after tumor resection. Clin Orthop Relat Res 1991;231–6. [CrossRef]

94. Winkelmann WW. Rotationplasty. Orthop Clin North Am 1996;27:503–23.