Reconstruction Following Tumor Resections in Skeletally Immature Patients

Abstract
Reconstruction options in children after bone tumor resection are as varied as they are challenging. Advances in biologic and endoprosthetic design have led to many choices, all of which must be considered in the context of prognosis, treatment limitations, and patient/family expectations. The current experience and results of limb-sparing surgery following bone sarcoma resection in growing children are discussed, including allograft, autograft, and metallic prostheses alone and in combination, especially as they pertain to the knee. In some cases, the ablative options of amputation and rotationplasty must be seen as equal and, at times, superior choices to limb salvage.

The treatment paradigm for the two most common primary bone sarcomas in children (ie, osteosarcoma and Ewing sarcoma) combines multiagent chemotherapy and wide surgical resection. For certain anatomic locations, radiation therapy may be the preferred local control method for Ewing sarcoma. Nearly 90% of patients with extremity bone sarcomas are considered candidates for limb-salvage surgery. With advances in endoprosthetic design and implant fixation, the ability to reconstruct osseous defects after oncologic limb-salvage resections with “off-the-shelf” modular implants has improved. Similarly, a greater understanding of bone and allograft healing has afforded opportunities to optimize biologic reconstructions after oncologic resections.

The peak incidence of osteosarcoma and Ewing sarcoma is in the second decade of life, during a time of accelerated skeletal growth. The overall survival rate from nonmetastatic disease is commonly >70% at 5 years. This combination of circumstances poses a tremendous challenge to the orthopaedic oncologist to provide durable reconstructions capable of acceptable function over a long period of time while maintaining leg-length equality. In addition to helping patients and families navigate the emotional and social burdens of a diagnosis of malignancy during the vulnerable adolescent period, equally important is weighing the technical considerations for limb-salvage reconstruction in the skeletally immature patient.

Evaluation, Staging, and Workup
The initial staging workup for a primary bone sarcoma routinely involves cross-sectional imaging of the chest and positron emission tomography or bone scan to screen for distant metastases. In addition, gadolinium-enhanced MRI is essential to evaluate the location of the metastases.
tumor relative to the surrounding anatomic structures and constraints. A scout coronal image of the entire limb is one technique to evaluate for skip metastases, which are present in 1.4% of all osteosarcoma cases. Because the presence or suspicion of a skip metastasis may change the decision for limb salvage or may substantially alter the resection plan, thorough evaluation is important.

Additional evaluation involves identifying the soft tissues that require resection to attain wide margins, including skin, muscle, tendons, ligaments, and vascular structures. Attention to detail on imaging may help the surgeon to identify the most appropriate reconstructive options and ensure optimal soft-tissue coverage. At the time of sarcoma resection, all tissues potentially contaminated at the time of prior biopsy should be widely excised together with the tumor mass. The potential dangers of a poorly planned biopsy are well-documented in the orthopaedic literature and may substantially complicate limb-salvage efforts. Before performing a biopsy, the need for soft-tissue coverage (eg, with muscle flaps, skin grafts) should be anticipated and incorporated into the overall surgical plan. Early recognition that a wide excision would compromise the pedicle to the optimal flap would dictate planning for another surgical approach or ensuring access to alternative soft-tissue coverage, if necessary. For young children, available allografts or endoprosthetic implants may be wider than the resected bone, further complicating tissue closure and coverage.

Leg-length Estimation

The greatest difficulty associated with oncologic resections in the growing child is negotiating the open physes. When the growth plate can be safely preserved, so are many of the options for ensuring limb-length equality in the skeletally immature patient. However, bone tumors often involve the metaphyseal region of long bones, and the adjacent growth plate frequently needs to be sacrificed to achieve local tumor control. Anticipating the remaining growth potential is an essential step for preoperative planning of limb-salvage surgery in skeletally immature patients.

The final limb-length deficit is calculated with the assumption of a normal contralateral growth rate. The amount of growth remaining at the resected growth plate and the patient’s skeletal age are also considered. Several methods are available to calculate the estimated discrepancy, including the Green and Anderson tables, the Moseley straight-line graph, and the multiplier method. The easiest approach is the estimation method that takes into consideration the normal growth rate per specific physis per year (eg, the distal femur grows at a rate of 0.9 cm per year). Currently, several computer applications are also available to facilitate these calculations.

When final estimated limb-length discrepancy at skeletal maturity is <2 cm, intervention is often not indicated. For discrepancies measuring 2 to 5 cm, our recommendation is to halt the growth of the contralateral side. Appropriate timing of epiphysiodesis requires performing serial growth calculations. For estimated differences >5 cm, the options include an extendible prosthesis or secondary limb lengthening. Although there is no agreed-on anticipated maximum limb-length discrepancy for which limb salvage is contraindicated, large potential discrepancies in young patients warrant strong consideration of amputation or rotationplasty.

Transphyseal Spread

For patients with metaphyseal tumors that preclude safe preservation of the physes, there may still be a benefit to epiphyseal preservation in an effort to preserve the joint. Although the physis was initially thought to be a robust barrier to sarcomas, further study has shown that >80% of high-grade metaphyseal osteosarcomas show some degree of transphyseal spread. The marrow margins of the tumor can occasionally be obscured on MRI scans by red marrow conversion in the setting of granulocyte-colony stimulating factor, which can mimic changes of intramedullary malignancy, especially on T1-weighted sequences. Fortunately, MRI is highly sensitive and specific for detecting tumor extension across the open physes (Figure 1).
Reconstructive Options

Physeal-sparing Resection

Diaphyseal tumors can often be resected with safe sparing of the physis, thus avoiding some of the concerns about limb-length inequality. Although intercalary endoprostheses are available, these tumors are ideally suited for biologic reconstruction. The literature regarding optimal reconstructive options is limited and often reflects the biases of the treatment centers. Small segmental resections can often be treated with intercalary allograft or bone transport, whereas intercalary defects measuring >10 cm may best be treated with a vascularized autograft.9

In their review of retrieved human allografts, Enneking and Campanacci described the healing response at the interface between host bone and allograft. Although apposition of bone was noted along the external surface and some internal repair that was largely limited to the interface, they found minimal revitalization of the allograft.10 Mankin et al11 showed that these necrotic allografts can be complicated by infection (11%), nonunion (17%), or fracture (19%). For intercalary resections, intramedullary nail fixation may lower the risk of allograft fracture, although conflicting studies as to whether this increases the rate of osseous nonunion are reported.12,13

In a subsequent study of children and adolescents treated with plate fixation, those stabilized with locked plates appeared to have a better rate of union (75%) compared with nonlocked plates (55%).14

Among the benefits of vascularized fibular autografts is the introduction of viable bone, potentially decreasing the incidence of infection,15,16 and improving the rate of union (89% to 93%).15,17 Given that many diaphyseal resections are done in patients requiring adjuvant chemotherapy, which may double the rate of allograft nonunion,18 techniques to effectively improve the healing rate in these patients are needed.

Over time, the vascularized autograft can hypertrophy, providing structurally sound living bone that is capable of remodeling (Figure 2). Although vascularized grafts can also fracture (rates range from 13% to 52%),19 the viable bone has better healing potential than does a necrotic allograft. In an effort to augment structural stability before hypertrophy, vascularized fibular grafts are often combined with allografts, wherein, for example, the autograft can be inset into the reamed medullary canal of a bulk allograft.20,21 (Figure 3). One technique uses a trough or window to allow for the nutrient vessel to remain without compression (Figure 4). The addition of the allograft allows plate fixation onto the surrounding allograft.
scaffold, thus avoiding any disturbance of the underlying autograft.

After diaphyseal resections, the intercalary bone graft is placed in an effort to minimize disturbance of the physis. However, for many of these patients, adequate skeletal fixation requires instrumentation that extends to the epiphysis. A locking plate construct that crosses the physis can functionally act as an epiphysiodosis. This can potentially be alleviated by removing the epiphysial screws from the construct after osseous union, allowing growth to resume at that location.

Although the bulk of the fibula is generally considered to be expendable, making it a highly useful source for autograft, its harvest is not without potential complication. Up to 36% of patients will experience some donor site morbidity, such as peroneal nerve dysfunction or claw toes. 17

The length of the residual distal fibula, together with the patient’s age, can help predict the likelihood of postoperative ankle instability and the need for distal tibiofibular synostosis. Less predictable is the risk of growth arrest at the distal tibia in the skeletally immature patient, potentially resulting in delayed valgus ankle deformity. 22

Transepiphysal Resection

For patients with metaphyseal lesions that preclude the safe avoidance of the growth plate, there may still be a benefit to preserving the articular surface. Cañadell et al 23 initially described using external fixation for physeal distraction before limb salvage in skeletally immature patients to improve or increase the margins and allow joint-sparing procedures. External fixation was then used as the main tool for limb reconstruction with distraction osteogenesis/bone transport to fill in the defect. 23

The concerns regarding distraction osteogenesis during chemotherapy include the risk of pin-site infection and loss of fixation and the quality of the regenerate. A few animal studies failed to show any delays in the development of new bone. 24 Tsuchiya et al 25 studied the safety of external fixation after limb salvage in patients receiving neoadjuvant chemotherapy. The cohort of 19 patients consisted of a group of patients who underwent distraction osteogenesis with external fixation and another group who underwent vascularized fibular grafting with an external fixator used as the only fixation method for reconstruction. The overall incidence of pin-site infection was 4.7% (4.9% for wire, 4.6% for half pins). In their study, postoperative chemotherapy did not adversely affect the union or hypertrophy of the vascularized fibular graft, and only minimal effects on distraction osteogenesis were seen. 25 Kapukaya et al 26 reported mostly good and excellent outcomes with distraction osteogenesis in this setting and failed to find any major adverse effects on the quality of new bone formation.

Transepiphysal resection in skeletally immature patients presents several technical challenges. This is a clinical situation that highlights some of the most intriguing advances in musculoskeletal oncology. Intraoperative image guidance, whether by fluoroscopy, CT, or computer navigation, is essential to guiding the resection plane with precision and accuracy, given the small margin for error. With the introduction of three-dimensional printing, research has been undertaken in patient-specific resection guides for improved accuracy of osseous cuts for use in patients for whom resection margins allow fixation of these guides directly onto the bone. 2 Multidimensional CT-based computer modeling of the area of anticipated bone resection and available banked allografts afford the ability to optimize the size- and shape-match of the graft. 27 Even after an optimal resection, limited bone remains in the epiphysis for skeletal fixation, and careful attention to soft-tissue reconstruction is important to the success of the procedure. 28

In the most comprehensive series of transepiphysal reconstructions in skeletally immature patients with osteosarcoma, Aponte-Tinao et al 29 reported no local recurrences within the epiphysis in their highly selected cohort of 35 patients; however, a complication developed in 54% of patients, and 14% required eventual resection of the epiphysis. Despite these technical difficulties and high complication rates, those who underwent successful preservation of the epiphysis reported excellent functional outcomes that continued to improve at long-term follow-up.
Intra-articular Resection

For children in whom joint preservation cannot be performed safely, biologic articular reconstruction may be an option. With resections of the proximal tibia, extensor mechanism function is improved with tendon-to-tendon healing, which can be achieved using a proximal tibial osteoarticular allograft with preserved soft-tissue attachments. Therefore, proximal tibial resections in children are a common indication for osteoarticular allograft placement (Figure 5). One of the principal benefits of osteoarticular allograft in this setting is the ability to avoid a stemmed implant across the distal femoral physis, which would typically be done during endoprosthetic reconstructions around the knee. A major limitation of this technique is the lack of available allograft tissue for this age group.

Although osteoarticular allografts also help build bone stock in young patients who will likely require further surgical procedures, the allograft bone remains necrotic. Furthermore, allograft bone cannot be lengthened, thus resulting in an anticipated limb-length inequality. These bulk allografts also have high rates of infection or fracture, although introduction of polymethyl methacrylate into the medullary cavity has been shown to decrease the rate of fracture in irradiated bulk allografts. Intramedullary cement, while potentially beneficial for these purposes, may limit future arthroplasty options.

Because of excision of all ligamentous and soft-tissue constraints about the joint, instability is a common complication after osteoarticular allograft reconstruction. This instability, together with cartilage necrosis and a marked rate of articular collapse, results in articular degeneration in up to 72% of patients. Many of these patients undergo revision with preservation of the allograft as an allograft-
prosthetic composite. The use of chondroprotection during freezing of osteoarticular allografts has shown improved viability in animal models, although translation of this method for preventing degeneration in human grafts has yet to be demonstrated.

**Endoprosthetic Reconstruction**

With modern, off-the-shelf modular implants, the preferred reconstruction after intra-articular oncologic resection is with endoprostheses. Multiple options exist for stem fixation in endoprosthetic implants, with variability in the reported experiences between centers. Among the benefits of cemented fixation is immediate stability, allowing for full weight bearing after surgery. Although this may work well for many skeletally immature patients, the very young child may have a medullary diameter that is too small to allow for a stem with an adequate cement mantle. Institutions favoring fixation with a cemented stem have reported excellent long-term outcomes. However, others prefer press-fit stems, which may help preserve diaphyseal bone stock in the event of future revision reconstructions. Because of concerns over the rate of bony ingrowth for press-fit fixation during adjuvant chemotherapy, a postoperative period of protected weight bearing may be required.

The goal of limb-salvage reconstruction is to provide a functional and durable limb, with an expectation that these young patients will remain active. One of the consequences of reconstruction is the eventual need for revision reconstruction. In an attempt to decrease periprosthetic osteolysis and to preserve bone stock in the reconstructed limb, a method of fixation that uses compressive osseointegration to promote implant stability has been developed. Approximately 400 to 800 pounds (181 to 363 kg) of compression is applied between the implant and the end of the bone, using Wolff's Law, rather than stress shielding, to promote hypertrophy of the bone at the bone-prosthetic interface. Intermediate to long-term follow-up has shown favorable results, with a low rate of aseptic loosening. With only a short stem (ie, anchor plug), the adequate amount of residual host bone necessary for fixation is less than that needed with cemented or press-fit stems. Most often, restricted weight bearing is expected for up to 12 weeks after surgery.

In the growing child, resections that sacrifice the physis will result in limb-length inequality. Although inserting longer implants may be an option at the time of reconstruction, concerns for soft-tissue tension and stiffness, wound healing, and the compliance of neurovascular structures in the setting of chemotherapy limit the amount that the limb can be acutely lengthened. For younger patients in whom contralateral epiphysiodesis is less favorable, a growing endoprosthesis may be appropriate. By using a variety of

**Figure 7**

A, AP radiograph of the femur showing an extensible distal femoral prosthesis that uses manual distraction with the addition of 1-cm blocks. B, AP radiograph of the femur demonstrating 3-cm expansion of the device in the diaphyseal component (arrow).
designs, these devices allow for extension over time to match the length of the contralateral limb. The length of the bone that is resected dictates the amount that can be extended, which for younger patients with relatively small resections, may still be inadequate for the anticipated limb-length inequality.

Most designs of extendible endoprostheses require a surgical approach to reach the extension mechanism via a worm-gear mechanism or with insertion of expansion clips after manual distraction of the prosthesis (Figures 6 and 7). Noninvasive extendible devices, which use an external magnet that drives the internal extension gear, have also been developed. The extension of the device can usually be comfortably completed in the office, without anesthesia, and can be done over the course of smaller incremental lengthenings. Furthermore, the avoidance of repeat incisions lowers the risks of infection and wound complications. The first noninvasive extendible implant for use in the United States was the Repiphysis Limb Salvage System (Wright Medical Technologies). Studies have shown high rates of complications and early loosening with this implant system.47,48 In terms of short- to intermediate-term results, the Juvenile Tumor System Extendible Implant (Stanmore Implants) appears to be more favorable, although revision rates for infection, extension complications, and implant failure are still high. At a mean follow-up of <5 years for reconstruction of the distal femur, reported outcomes indicate that nearly half of patients treated with noninvasive extendible endoprostheses required revision of components.39,40 The results for invasive expandable implants are historically somewhat better, with favorable emotional and physical results, but they still have a complication rate of up to 42%.41

For proximal femur or proximal humerus reconstructions, intra-articular resections may be performed as a hemiarthroplasty, thereby avoiding instrumentation across the joint. Bipolar hemiarthroplasty of the hip in children with open triradiate cartilage results in premature arrest of the normal deepening and enlargement of the acetabulum, resulting in a relative superolateral migration of the hip center.42 For reconstructions about the knee, however, most implant systems require instrumentation across the joint for a congruent articulation. This introduces a potential disruption of the adjacent physis, which can be mitigated by placement of a highly polished press-fit stem in the central portion of the physis to allow continued physeal growth43-45 (Figure 8).

Amputation

Although chemotherapy has permitted limb salvage to become the primary surgical option for local control of extremity malignant bone tumors, amputation is still needed in approximately 10% of cases to obtain adequate local tumor control. Although amputations are often less technically challenging than limb-salvage procedures, complications include phantom pain, bleeding, infection, bone overgrowth, soft-tissue stump migration, and muscle imbalance. Amputation leads to a
A major increase in energy expenditure and metabolic demands during ambulation. More proximal amputations incur higher energy demands. For example, whereas a Syme amputation increases energy demands by 15%, a transfemoral amputation increases demand by >50%.46

Bony overgrowth is also a common complication (incidence, 5% to 40%) after amputation in children. It occurs more often in children aged <10 years, especially in those who have had an amputation through the diaphysis of the tibia/fibula and humerus. Overgrowth may lead to skin perforation, pressure ulcers, and difficulty fitting to the prosthesis. Several authors recommend a disarticulation or osteomyoplasty (ie, Ertl procedure) to avoid overgrowth.47

Rotationplasty

Rotationplasty was originally described by Borggreve48 in 1930 for a patient with severe limb deformity secondary to tuberculosis. In 1950, Van Nes49 popularized the procedure for management of proximal femoral focal deficiency associated with severe limb-length discrepancy. Rotationplasty was initially used as an alternative to above-knee amputation for the treatment of malignant bone tumors in the 1970s. With the advent of limb-salvage techniques, rotationplasty has become less common, but it remains an option for skeletally immature patients with bone sarcomas around the knee and after failed limb-salvage procedures. The main functional advantage of rotationplasty relies on the preservation of the ankle joint, which acts as a new knee joint. This allows less energy expenditure during ambulation compared with the amount of expenditure during ambulation in above-knee amputation.50 Rotationplasty also avoids phantom pain and decreases the need for further surgeries for limb-length discrepancy or revision for loosening or fracture of the endoprosthesis or other limb-salvage modality, especially in highly active, growing children. Rotationplasty is particularly favored in patients with an extensive soft-tissue mass, intra-articular extension of tumor, abnormal fractures, or sizable anticipated limb-length discrepancy. The vessels may be resected and anastomosed if necessary to achieve adequate margins. For the success of the surgery, the only structure that needs to be left intact is the sciatic nerve and its branches (Figure 9).

Rotationplasty is likely less commonly performed because of concerns about the unusual appearance of the rotated limb. Using the Medical Outcomes 36-Item Short Form Survey in 20 patients, Forni et al51 reported on the long-term quality of life of patients after rotationplasty at an average of 17 years after surgery. The quality-of-life scores were nearly the same as those of the general population. The authors also reported on interviews conducted with subjects aged 17 to 38 years who had undergone rotationplasty, and the results showed relational and emotional difficulties in adolescence, which were often overcome in adulthood, and the importance of a cosmetic and functional prosthesis, as well as family support.

Figure 9

A, Intraoperative photograph of a rotationplasty procedure. The sciatic nerve and femoral vessels are the only structures that remain in continuity after tumor resection. B, Clinical photograph of a healed rotationplasty.
Advances in biologic and endoprosthetic design have led to many choices, all of which must be considered in the context of prognosis, treatment limitations, and patient/family expectations. It is incumbent on the treating surgeon to remain grounded in realistic expectations for patients in whom long-term cure is expected. The ablative options of amputation and rotationplasty must be seen as equal, and in some cases, superior choices to limb salvage.

References

Evidence-based Medicine: Levels of evidence are described in the table of contents. In this article, reference 35 is a level III study. References 19, 21, 28, 29, 32, 36-38, and 54 are level IV studies. References printed in bold type are those published within the past 5 years.


Summary

Reconstruction options in children after bone tumor resection are as varied as they are challenging.


