Limb Salvage in Paediatric Bone Tumours

Michael Parry[1], Robert Grimer[1]

Abstract

Significant progress has been made in the management of paediatric osseous sarcoma. Where historically this diagnosis conferred a dismal prognosis, modern strategies of oncological management have resulted in significant improvements in disease free survival. These improvements have resulted in a broadening of the feasibility of limb salvage, which, in the paediatric population, presents its own unique challenges. Treatment must prioritize life over limb and not compromise local control for the advantage of cosmesis, limb length or function. Limb salvage, where possible, offers distinct advantages over conventional amputations and with the advent of modern techniques and technologies, should always be a consideration in the paediatric sarcoma population.

Keywords: Limb salvage, paediatric sarcoma.

Introduction

Primary malignant tumours arising from bone are relatively rare in the paediatric and adolescent population, accounting for only 6% of childhood malignancies. Of these, the majority (>90%) comprises osteosarcoma and Ewing's sarcoma. Other bone sarcomas including chondrosarcoma, malignant fibrous histiocytoma, fibrosarcoma, malignant giant cell tumours, and adamantinoma can occur in the paediatric population although their incidence is relatively low. In these rare tumours, surgery is the first choice for local control. Historically, an extremity sarcoma in a child conferred a dismal prognosis. However, advances in imaging modalities, greater understanding of the role of local control, and the use of multi-agent chemotherapy, has resulted in a significant improvement in overall survival. Such advances have resulted in an increase in 5-year survival from 10-20% to 60-70% with modern techniques. Thanks to these improvements in overall survival and a groundswell of interest and advances in technology, limb salvage is now regarded as the gold standard of treatment for those presenting with osseous extremity sarcoma. Advances in bone banking and an appreciation of the behavior of prosthetic replacement have improved surgical outcomes in limb salvage, though they have created their own complications. The aim of this review is to explore the advances in limb salvage surgery for osseous sarcoma in the paediatric population.

Patient Assessment and Diagnosis

Patients presenting with a suspected sarcoma should be managed in a specialist institution with the expertise and multi-disciplinary facilities necessary for the holistic care of the patient throughout their cancer journey. This is no more apparent than in the paediatric population where treatment decisions must be agreeable not only to the patient but also to their parent or carer.

In all patients, a detailed history and examination is mandatory. Whilst the majority of sarcomas are sporadic, rare familial conditions, including Retinoblastoma and Li Fraumeni syndrome, should be identified. The physical examination must include assessment not only of the lesion but also the distal neurovascular status of the limb.

Radiography must include a plain radiograph of the affected bone or limb segment as this will form the basis of the diagnosis. Further, detailed cross sectional imaging, most commonly with magnetic resonance imaging (MRI) will allow local staging. Systemic staging of the disease necessitates computerized tomography (CT) of the chest, as well as skeletal imaging, either in the form of a technicium Tc-99m scan, or whole body MRI. Systemic staging may include positron emission tomography (PET) in conjunction with a CT scan, though this is dependent on local and institutional guidelines.

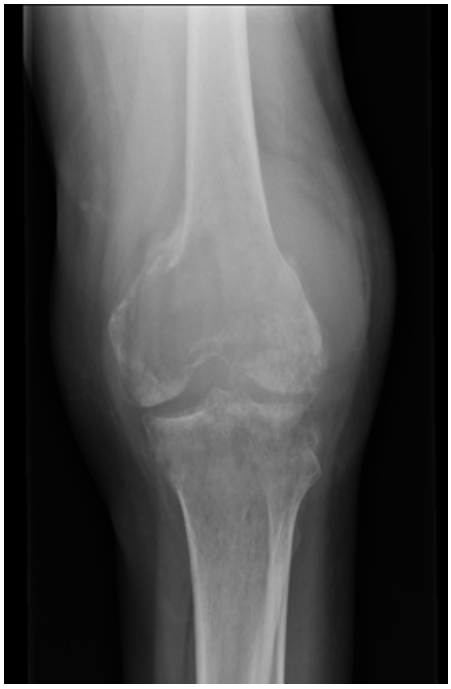
Biopsy remains the cornerstone of confirmation of diagnosis for any suspected malignancy arising from bone. Improperly performed biopsies can result in a delay in treatment, hinder subsequent attempts at limb salvage, and result in an increase in local recurrence. MRI prior to biopsy helps identify the optimal position for biopsy and avoids distortion of the imaging by post-biopsy changes. The biopsy should be performed in such a way that the tract can be completely excised at the time of definitive resection and should be

[1]The Royal Orthopaedic Hospital, Birmingham, UK.

Address of Correspondence
Dr. Michael Parry.
Royal Orthopaedic Hospital NHS Foundation Trust
Bristol Road South ,Northfield, Birmingham
B31 2AP, United Kingdom
Email: michael.parry3@nhs.net


Dr. Michael Parry


Dr. Robert Grimer



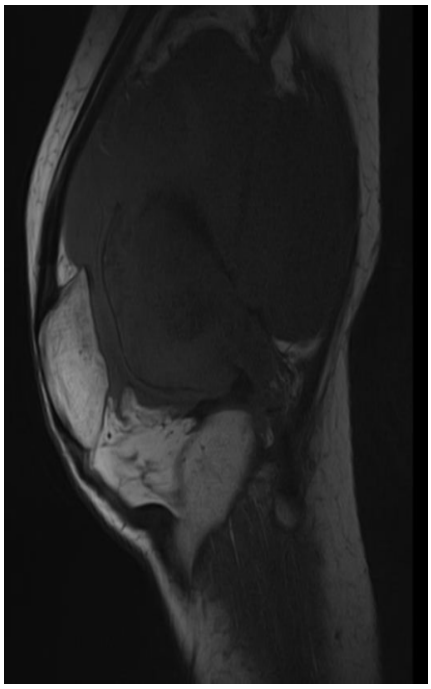


Figure 1: Adolescent patient with a three month history of left knee pain and swelling. Imaging shows a destructive lesion of the distal femur. MRI shows tumour in the knee and around the neurovascular bundle. Biopsy confirmed osteosarcoma. The patient did not respond to chemotherapy without apparent response. The only safe surgery for this is amputation.

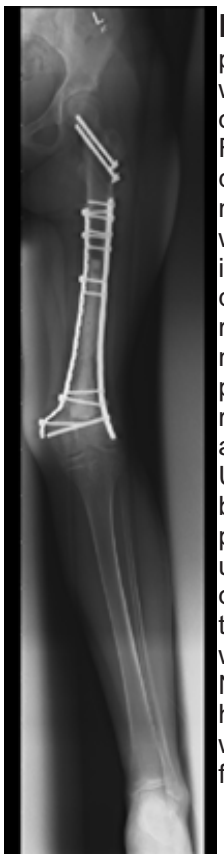


Figure 2: 8yr old patient presented with Ewings sarcoma of the mid femur. Following chemotherapy, the middle of the femur was excised, irradiated, filled with cement and then reimplanted with medial and lateral plates. The distal resection was just above the epiphysis. Union was achieved by 4 months. The patient suffered an undisplaced fracture of the neck of femur two years later, fixed with two screws. Now, aged 20, she has a 4cm short leg with normal knee function.

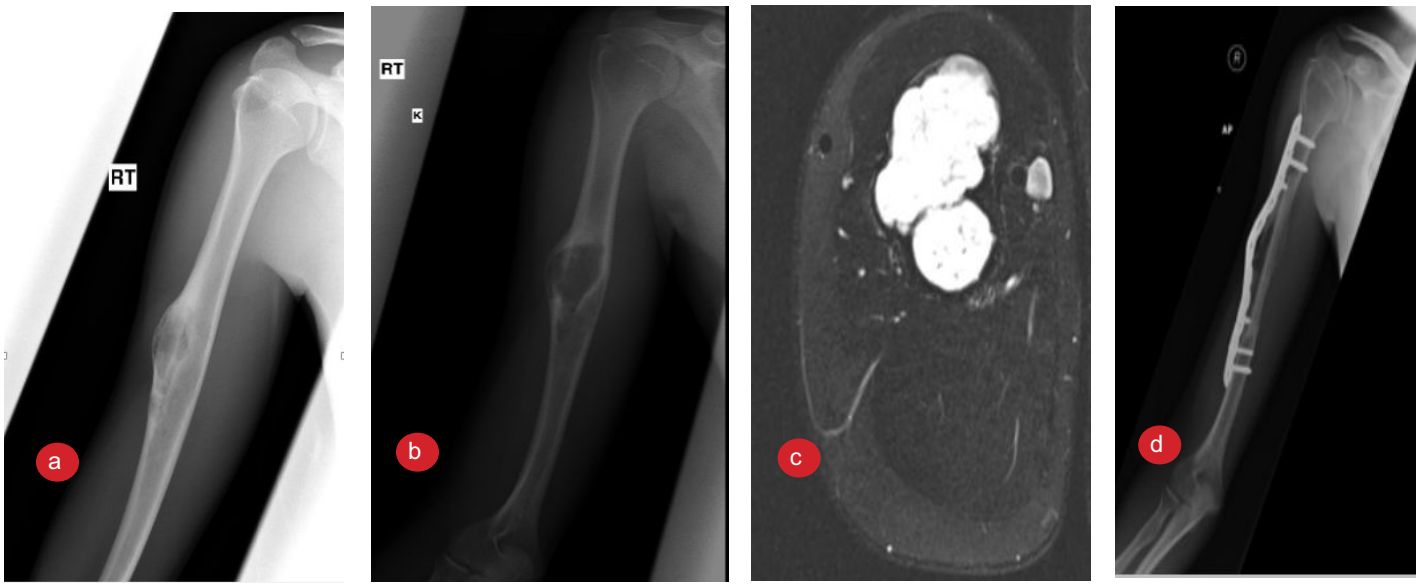
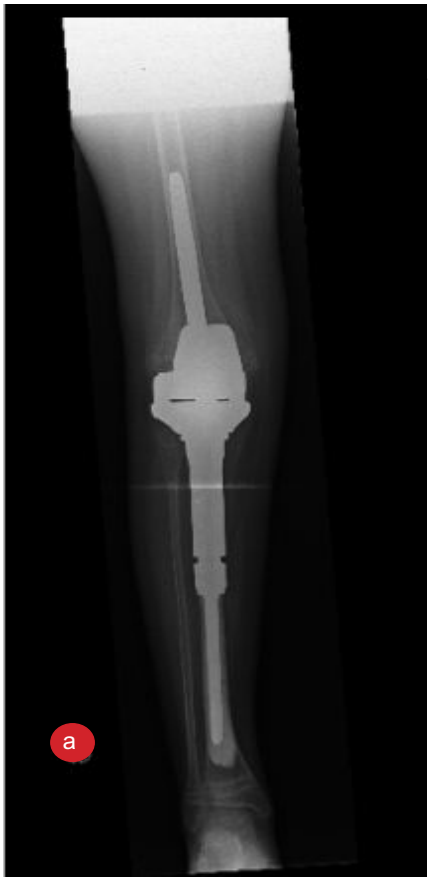


Figure 3: 15 year old patient presented with a lump on his arm. Initial XRay (a) showed a lesion in the mid humerus and biopsy suggested a benign enchondroma. This was watched but four years later it rapidly increased in size (b and c), Biopsy now showed a low grade chondrosarcoma. The mid humerus was removed, the tumour curetted and the bone sterilised with radiotherapy. It was replaced and augmented with a fibula graft. (d) Normal function was restored within 9 months.

performed by a surgeon familiar with the techniques of limb salvage. The use of image guidance with ultrasound or CT is especially pertinent in the paediatric population where considerable contamination can occur with open biopsy techniques.

General Treatment Considerations

It is imperative that discussions regarding treatment are conducted in the setting of a multi-disciplinary team including



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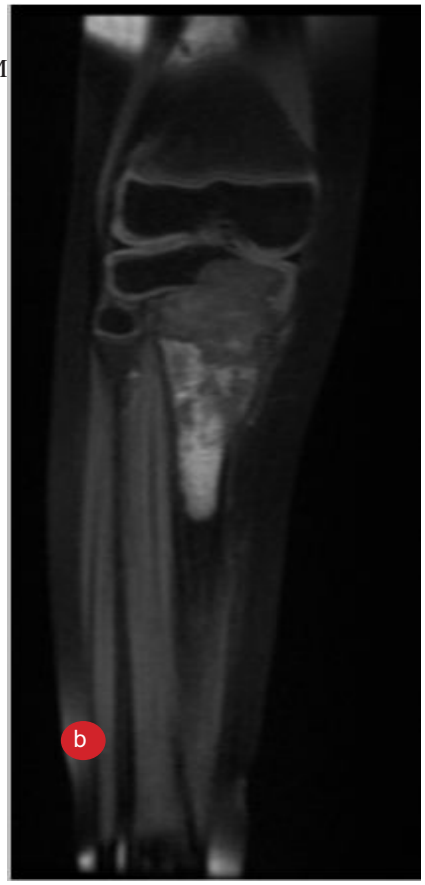

Figure 4: A 12 year old boy with an osteosarcoma of the proximal tibia growing into the epiphysis but sparing the knee joint (a). Following neo-adjuvant chemotherapy, the tumour was excised and reconstructed with a minimally invasive extendible proximal tibial replacement (b).

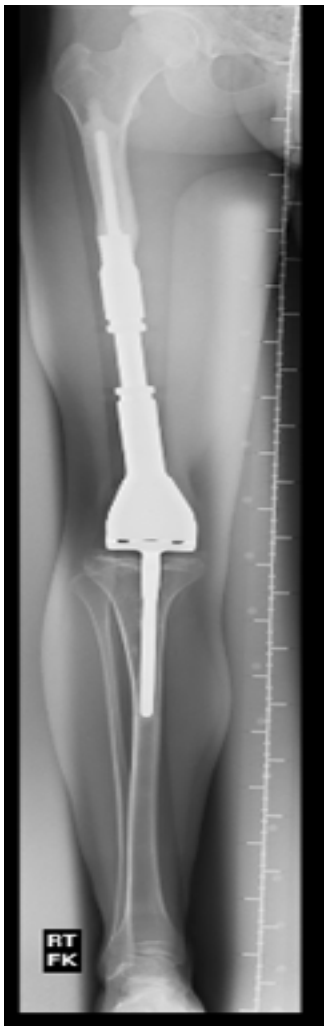

Figure 5: The case of a 12 year old boy who had resection of the right distal femur for an osteosarcoma in 2005. This was reconstructed with a rotating hinge non-invasive extendable prosthesis. After 10 years, the prosthesis has been lenghtened by 55 mm and the patient has an excellent function at the knee.

specialists in paediatric oncology, radiology, histopathology and orthopaedic oncology surgery. Having established the diagnosis, in terms of histological type and grade, and staged the local and systemic burden of disease, discussion turns to local control. The timing of local control varies dependent on diagnosis and stage. Most strategies utilize systemic chemotherapy prior to definitive local control. This allows the treatment of metastatic or suspected micro-metastatic disease to be instigated immediately. This time lapse allows careful planning of the definitive surgical resection, allowing time for custom made implants or grafts. It also allows an assessment to be made of the tumour response to neo-adjuvant therapies, which often guides adjuvant therapy following tumour resection. In some cases, neo-adjuvant therapy results in a dramatic change in the tumour facilitating subsequent resection. The modality for local control must take into consideration patient, tumoural, socio-economic, cultural and technical biases.

Amputation versus Limb Salvage

Whilst no absolute contraindications to limb salvage exist, the involvement of neurovascular structures which preclude attainment of a clear margin without significant impairment of limb function, and very young skeletal age, should point away from limb salvage as the definitive local control. Relative contraindications include factors resulting in a delay in reinstating systemic therapy, including infection and post operative wound complications, and factors most likely to result in an increase in local recurrence, including tumour bed contamination from inappropriate biopsy, expected positive surgical margins and pathological fracture (Fig. 1).

Patient wishes must be respected when considering amputation or limb salvage. The majority of studies comparing function in these two treatment groups have looked at tumours of the distal femur. No statistically significant difference has been demonstrated in the overall or disease specific outcomes between these two approaches, which is a manifestation of appropriate patient selection. According to the available outcome scores, function following amputation is comparable to that of limb salvage, with comparable psychological end points. Patients with limb salvage will often have a superior cosmetic result but often at the expense of endurance in certain physical activities. Patients undergoing limb salvage will undergo more surgical interventions than

their amputation counterparts and patients and their families should be made aware of the lifetime of surveillance and repeated surgical interventions at the outset. However, financial considerations should not sway the intervention, especially as amputation patients will require a greater lifetime expense than their limb salvage counterparts.

Limb Salvage Surgery

When considering surgery for local control in osseous malignancies of the immature skeleton, consideration must be given to the tumour location and the sensitivity to oncological treatment modalities. For tumours sensitive to chemotherapy and radiotherapy, (especially Ewings sarcoma), in challenging locations where surgical resection will result in unacceptable morbidity or an uncontaminated margin will be difficult to achieve, then non-surgical interventions may be more appropriate. Alternatively, for tumours not sensitive to radiotherapy, such as osteosarcoma, surgical resection may be the only option for local control, regardless of the morbidity. Surgery for the primary tumour and for metastatic deposits should be considered wherever possible. The aim in all surgery is to obtain as wide a margin of clear tissue as possible around the tumour. The better the response of the tumour to neoadjuvant treatment the safer limb salvage surgery becomes. Local control is indispensible for the cure of patients with Ewing's sarcoma. Intralesional resection is associated with an increased risk of local recurrence and distant metastases.

Resection Without Reconstruction

For tumours arising in dispensable bones in the immature skeleton, including sections of the ulna, the scapula, the sacrum, the pelvis and fibula, local control can be achieved through excision without reconstruction. Excellent functional outcomes can be achieved without reconstruction, more so in the adaptable paediatric population.

Resection and Reconstruction

Biological Reconstruction

Autograft The large bony defect created following resection of an osseous malignancy often necessitates reconstruction for preservation of function and continued skeletal growth. The use of non-vascularised autologous structural bone graft dates back 100 years , whilst the use of a vascularized fibula graft was first described by Taylor in 1975. The blood supply of the vascularized graft is preserved by anastomosing its feeding vessel to a host artery. The graft subsequently undergoes revascularization from this vessel and from the surrounding vascular bed. Since its first description, this technique, as well as the use of non vascularized grafts, has been extensively described and applied. The technique lends itself best to reconstruction of intercalary long bone defects, or for proximal humeral osteoarticular reconstruction where the fibula provides not only structural support but also allows longitudinal growth of the limb segment from the proximal physeal plate. Special consideration should be given to resection of pelvic sarcomas where autograft reconstruction is being considered. An option for reconstruction in the adolescent age group, at or approaching skeletal maturity, is resection, extracorporeal sterilization and reimplantation. This has been reported as a viable method for reconstruction. Indeed, in their latest series reporting the use of this technique, Wafa et al reported a successful outcome in patients as young as 8 years old. This technique can also be applied to other body sites, particularly for intercalary reconstruction (Figs. 2 &3).

Allograft Improvements in tissue banking have allowed an expansion in the use of cadaveric osseous and osteoarticular allografts. Grafts are harvested and sterilized either by freezing or irradiation and can be offered on a custom made, size matched basis. There are mixed reports on the viability of articular cartilage following sterilization and the cadaveric bone itself is incorporated at best only moderately at osteosynthesis sites and beneath the periosteal sleeve, making the allograft at best a biomechanical scaffold. Depending on the site of reconstruction, up to 50% of patients undergoing allograft reconstruction can expect at least one complication, including infection, non-union or graft fracture. Some have reported infection rates following allograft reconstruction to be twice that seen following reconstruction with an endoprosthetic replacement. In spite of these potential problems, patients who avoid complications following allograft reconstruction function at a high level without the requirement for repeated revision procedures seen in endoprosthetic replacement.

In the case of adamantinoma and osteofibrous dysplasia like adamantinoma of the tibia, resection and reconstruction can be achieved either without reconstruction in the case of small, unicortical lesions, or with reconstruction using allograft, or autologous fibula graft. The fibula can be transferred and stabilized either in conjunction with a tibial allograft stabilized with plates or with the assistance of a ring external fixator.

In cases of diaphyseal resections, reconstruction can be achieved with intercalary allograft where the native joint above and below the lesion can be preserved. In many cases, particularly in Ewing's and osteosarcoma, the tumour extends to the metaphysis, sparing the physis. Careful dissection can allow removal of the tumour without injury to the physis, preservation of the native cartilage and ligamentous attachments. Reconstruction of the diaphyseal defect with an intercalary allograft stabilized with an intermedullary nail through the centre of the physis allows continued growth at the physis. Incorporation of the allograft can be augmented by the addition of a vascularized fibula graft within the allograft. For tumours involving the distal femur or proximal tibia in young patients, an alternative option for reconstruction, preserving the foot, is an intercalary resection, and tibial turn-up (Van Nes) arthroplasty. The residual limb is rotated through 180o, the ankle joint now forming the novel knee joint. The resultant limb has the cosmetic appearance of an above knee amputation whilst allowing the capacity for longitudinal growth, if the proximal tibial physis has been preserved. Following rotationplasty, a prosthesis can be worn at the knee allowing ambulation. Gait analysis demonstrates improved kinematics when compared to a

conventional above knee amputation. Careful consideration should be given not only to the technical demand of the procedure, but also the psychological impact on the patient and family of the disfiguring but highly functional procedure. The fact that the patients have no phantom pain is a distinct advantage over amputation at a similar level.

Non-Biological Reconstruction

Significant advances have been made in the design and manufacture of endoprostheses in the last 30 years. The advent of neo-adjuvant chemotherapeutic regimens has allowed an acceptable time lag between diagnosis and local control which allows for the manufacture of custom made endoprostheses based on the patients' particular anatomy without delaying treatment. Primitive devices suffered from errors in manufacture resulting in implant fractures and early loosening with non-rotating knee prostheses. The current generation of endoprostheses offer an attractive life span for the majority, failure largely attributable to stress shielding in long stem endoprostheses and particle-induced osteolysis due to wear at the bearing interface. Failure is largely dependent on anatomical location, with proximal humeral and proximal femoral devices faring best, whilst distal femoral and proximal tibial prostheses perform less well. Patients with endoprostheses will undoubtedly require revision surgery within their lifetime, each time requiring greater osseous and soft tissue resection. The risk of infection remains high and increases with each revision procedure, leading, in the worst-case scenario, to possible amputation. This risk is increased when radiotherapy is employed, particularly for endoprosthetic reconstruction of the proximal tibia.

In younger patients, with more than 2 years of growth remaining, the issue of limb-length equalization is a real concern, particularly at the distal femur, where the physis here accounts for the majority of longitudinal growth. In such patients, "growing" prostheses present an attractive answer. Prostheses incorporating a growing distraction device can allow predictable lengthening and equalization of leg lengths. Minimally invasive growing prostheses (Fig. 4), where the device is lengthened by a distraction screw, accessed through a small incision, can be used in patients where surveillance of local recurrence is expected to require MRI. In those where local recurrence is unlikely, a non-invasive growing prosthesis (Fig. 5) can be employed. In such devices, the prosthesis incorporates a magnetic motor activated by an external rotating magnet applied in close proximity to the limb. This overcomes the need for repeated surgical procedures, and the inherent risk of infection this carries. However, patients with such devices cannot undergo further MRI scanning due to the irreparable damage this incurs on the magnetic motor. Whichever endoprosthetic device is chosen, consideration should be given to the method of fixation to native bone. The failures of early devices, attributable to particle-mediated osteolysis, have, to a certain extent, been obviated by the use of hydroxyapatite collars, essentially sealing the medullary canal and implant-bone interface from particulate wear generated at the bearing surface[53,54].

Conclusions

The paucity of algorithms to guide treatment strategies in paediatric patients with osseous sarcomas is a reflection of the multifactorial influences that predict outcomes following resection. An appropriate strategy can only be achieved following careful consideration of oncological, pathological, surgical and patient factors. Whichever strategy is adopted, the sequence of priorities should always be first life, then limb, then function, with leg length discrepancy and cosmetic appearance affording lesser consideration. When true equipoise exists between limb salvage and limb sacrifice, in terms of overall and disease-free survival, consideration must be given to limb function not only in the immediate periods following reconstruction, but also for the entirety of the life of the patient. In the case of the paediatric population, this may exceed the professional lifetime of the treating surgeon.

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