# Bone Tumors; Limb Salvage

Stephen R. Cannon

## Introduction

Primary bone tumors in children are rare conditions, the upper limb being more rarely affected than the lower limb. The practicing general orthopedic surgeon may not see more than a single case of primary bone tumor over a 5 year period. This rarity makes the recognition—particularly of malignant bone tumors—extremely difficult. Not surprisingly, this leads to difficulties and errors being made in specific treatment. With the establishment of bone tumor/cancer registries, the incidence of malignant primary disease of bone can be seen to be around six cases per million per year. The incidence of osteosarcoma, the most common primary malignant bone tumor, showing peak risks of incidence related to puberty is greatest between 10 and 14 years for girls and between 15 and 18 years for boys [1] (Fig. 23.1).

The most common benign lesion of bone is undoubtedly the solitary osteocartilaginous exostosis (osteochondroma). This condition was first described by Sir Astley Cooper in 1918 [2]. Both solitary exostosis and multiple exostoses (diaphyseal aclasis) may lead to alteration of epiphyseal plate growth and joint subluxation and deformity [3]. Other common benign diseases affecting the skeleton include Ollier's disease [4] which, when associated with soft tissue hemangiomas is termed Maffucci's syndrome [5]. The true incidence of these conditions within the population is unknown, but it is well recognized that the enchondritic element of both syndromes may undergo malignant change [6]. The majority of giant cell tumors are found in the pelvis and lower limbs, although occasionally the distal and proximal radius may be involved. These lesions are, of course, exceedingly rare below the age of 15 years [7]. Of the primary malignant tumors of bone in childhood (Ewing's sarcoma and osteosarcoma), about 12–15 % of cases occur in the upper limb, including the clavicle.

When considering the diagnosis of a bone tumor, it is probably wise to keep the World Health Organization (WHO) classification in mind (Table 23.1). Lesions occurring predominantly in children are highlighted.

## Presentation

The diagnosis is often missed simply because it is not considered. It is important to realize that no part of the anatomy is exempt from a bone tumor, and every bone, every muscle and every nerve in all anatomical areas have been recorded as being sites of primary musculoskeletal tumors.

Children often present with symptoms that can be confused with other musculoskeletal injuries. Most children seek medical attention because of pain. The clinician should have a high index of suspicion for pain that is constant, unrelated to
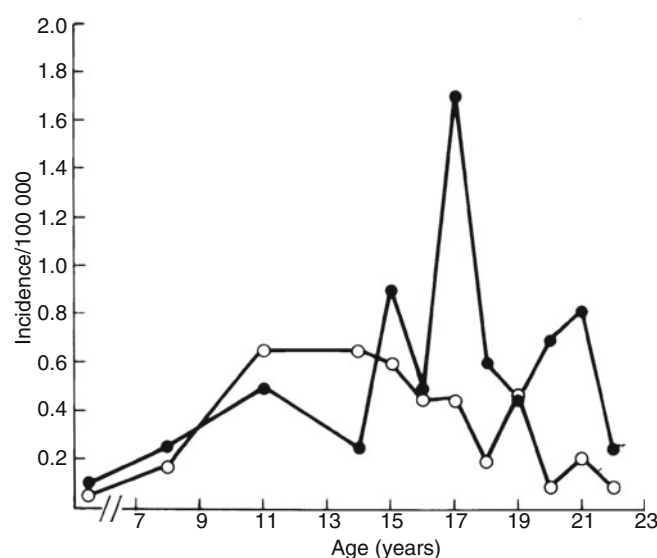


**Fig. 23.1** Incidence of osteosarcoma in boys and girls related to age

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**Table 23.1** WHO classification of common primary bone tumors

| A Bone-forming tumors | |
| --- | --- |
| i. Benign | Osteoma |
| | Osteoid osteoma |
| | Osteoblastoma |
| ii. Intermediate | Aggressive (malignant) osteoblastoma |
| iii. Malignant | Osteosarcoma |
| | (a) Central (medullary) |
| | (b) Surface (peripheral) |
| | Parosteal osteosarcoma |
| | Periosteal osteosarcoma |
| | High-grade surface |
| **B Cartilage-forming tumors** | |
| i. Benign | Chondroma |
| | (a) Enchondroma |
| | (b) Periosteal (juxtacortical) Osteochondroma (osteocartilaginous exostosis) |
| | (a) Solitary |
| | (b) Multiple hereditary |
| | Chondroblastoma |
| | Chondromyxoid fibroma |
| ii. Malignant | Chondrosarcoma |
| | Dedifferentiated chondrosarcoma |
| | Mesenchymal chondrosarcoma |
| | Clear cell chondrosarcoma |
| **C Giant cell tumor (osteoclastoma)** | |
| **D Marrow tumors (round cell tumors)** | |
| | Ewing's sarcoma of bone |
| | Neuroectodermal tumor of bone |
| | Malignant lymphoma of bone |
| | Myeloma |
| **E Vascular tumors** | |
| i. Benign | Hemangioma |
| | Lymphangioma |
| | Glomus tumor |
| ii. Intermediate | Hemangioendothelioma |
| | Hemangiopericytoma |
| iii. Malignant | Angiosarcoma |
| | Malignant hemangiopericytoma |
| **F Other connective tissue tumors** | |
| i. Benign | Benign fibrous histiocytoma |
| | Lipoma |
| ii. Intermediate | Desmoplastic fibroma |
| iii. Malignant | Fibrosarcoma |
| | Malignant fibrous histiocytoma |
| | Liposarcoma |
| | Malignant mesenchymoma |
| | Leiomyosarcoma |
| | Undifferentiated sarcoma |
| **G Other tumors** | |
| i. Benign | Neurilemmoma |
| | Neurofibroma |
| ii. Malignant | Chordoma |
| | Adamantinoma |
| **H Simple bone cyst** | |
| Aneurysmal bone cyst | |
| Classification of common primary bone tumors | |

activity, and is worse at night. The second most frequent complaint is of swelling. Of particular importance is the rate of tumor growth and whether there has been any relationship to trauma. The third more rare mode of presentation is the occurrence of a pathological fracture. Here, the presence of pain or swelling prior to the fracture is a most important clue to diagnosis. Constitutional symptoms of weight loss and occasionally fever are sinister observations, usually indicative of aggressive disease, often widespread but fortunately rare. Examination of the area complained of is the responsibility of the physician, and the features considered should be: first, is there tenderness and is there increase in the skin temperature? If there is a visible mass, how big is it? Has it changed in size since first noted? The physician should take appropriate measurements. Adjacent joints should be examined for the range of movement and the limb assessed for signs of muscle atrophy. The neurovascular status of the extremity involved should also be assessed. A complete physical examination should also be done, with particular reference to the regional lymph nodes and examination of the chest and abdomen where appropriate. Only after a very thorough history and careful examination should the next investigation, a plain radiograph, be performed.

## Radiographic Investigations

The single most important investigation in a suspected bone tumor is the plain radiograph. This investigation may be diagnostic in itself and direct further treatment without additional investigation or indeed the radiograph may alert the surgeon to the possibility of a bone tumor being present. It is also important to emphasize that the radiologist is not a clinician in his own right and requires appropriate information of what the clinician suspects in order to give the best service. The radiograph should be taken in two views at right angles to each other, and when a lesion is recognized the following helpful diagnostic exercise should be undertaken.

1. What is the anatomical site of the lesion? Which bone is it in? Is it in the epiphysis, metaphysis, or diaphysis? Is it in the medullary canal or is it in the cortex, lying on the cortex or surrounding the cortex?
2. What effect is the lesion having on the bone? Is bone being destroyed? Is it a local destruction? Is it permeative or are there moth-eaten changes?
3. What is the bone doing in response to the lesion? Is there an endosteal reaction? Is there a periosteal re action? Is a Codman's triangle, a sunburst pattern, or onion-skinning appearance present?
4. Is there anything about the lesion which is characteristic of a specific tumor? Is it forming new bone? Is there calcification? Does it have a ground glass appearance?

This approach is important, particularly in instances where the initial diagnosis can be safely made on the plain

radiograph alone. Lesions which are inactive, i.e., those that have no symptoms and have a mature reaction around them, can often be observed. Biopsy is usually not necessary. Lesions which appear to be more aggressive, i.e., giant cell tumor or chondroblastoma, may require further evaluation with other radiographic techniques prior to discussing management. In deciding which radiological investigations to acquire, it is useful to communicate with the radiologist which question is being asked. The orthopedic surgeon requires information that answers four questions in order to stage the tumor within the limb.

First, what is the intraosseous extent of the tumor? Second, what is the extraosseous extent of the tumor and what proportion of the lesion is still sub-periosteal? Third, is there any involvement of the adjacent intra-articular structures? Fourth, is the neurovascular bundle involved in the tumor process? If the tumor is malignant, then the clinician needs to know if there is any other bony lesion elsewhere and also if there is any metastatic spread to the lung.

Radio-isotopic technetium 99 m bone scintigraphy can be used both to determine the activity of a primary lesion and to search for other bony lesions. Occasionally the technetium bone scan can reveal the intraosseous extent of a lesion as well as computed tomography (CT) or magnetic resonance imaging (MRI) scanning [8] (Fig. 23.2). Lesions which do not have increased activity on the bone scan are usually benign. The two exceptions to this general rule are myeloma and Langerhans' histiocytosis. Lesions which have increased activity may be benign or malignant. The intensity of uptake is not predictive as to the likelihood of malignancy. Classically, the bone scan appearances of osteosarcoma are of intense activity with an irregular outline [9]. Bone scintigraphy may also on occasion demonstrate pulmonary metastases in instances of osteosarcoma.

Computed tomography is a valuable noninvasive investigation which can determine not only the intramedullary extent of the tumor but also demonstrate extra-osseous extension and the degree of cortical destruction (Fig. 23.3). It may also be used in conjunction with contrast medium to outline the relationship of the tumor to adjacent vascular structures or indeed to represent the vascularity of the lesion itself; CT scan of the lungs is important for accurate staging. Typically, metastases are found in the sub-pleural position (Fig. 23.4), but in spite of the greater sensitivity of this technique the proportion of patients with nor mal chest radiographs at presentation who are subsequently shown to have lung metastases by CT scan is only 10–15 % [10].

Magnetic resonance imaging is now considered the most sensitive single method for assessing intramedullary involvement by tumor [11]. Although both CT and MRI can demonstrate the presence of extra osseous soft tissue extension, MRI is superior to CT in differentiating tumor from adjoining muscle [12, 13] (Fig. 23.5). However, MRI is not as accurate as CT in determining the relationship of a tumor to the cortex of a bone or in evaluating a lesion which is composed of dense bone [14]. In addition, there can be
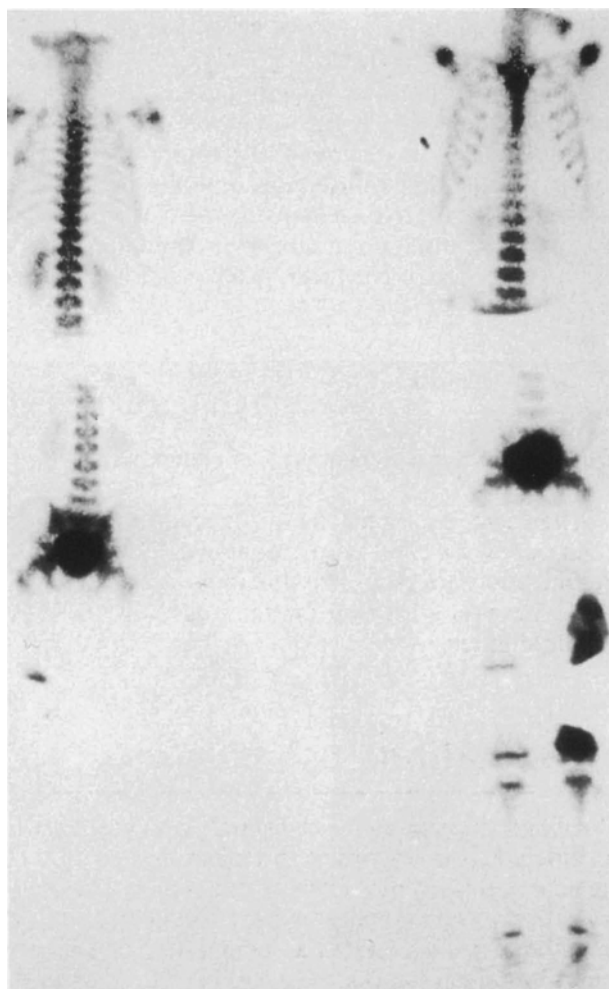


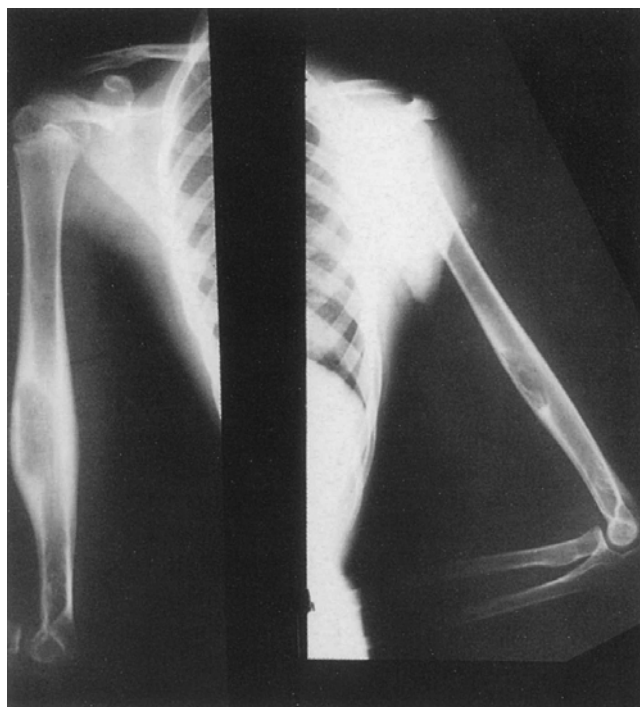**Fig. 23.2** Technetium bone scan of an osteosarcoma showing primary lesion and intraosseous extent



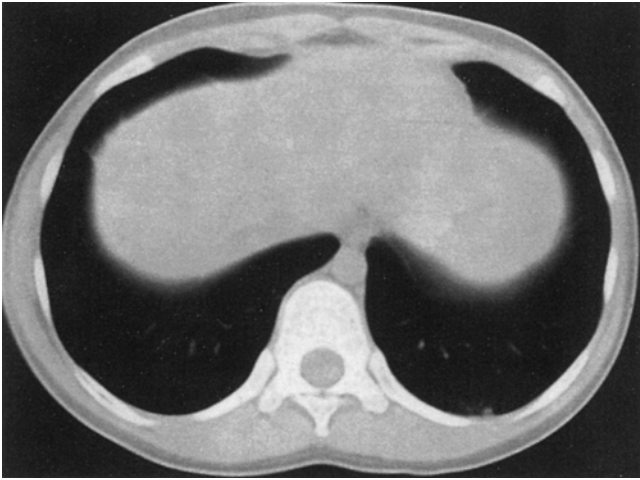**Fig. 23.3** Ewing's sarcoma showing cortical destruction

**Fig. 23.4** CT scan chest showing multiple subpleural and parenchymal metastases



**Fig. 23.5** MRI scan of Ewing's sarcoma showing large extraosseous mass

considerable difficulty in differentiating between tumor and peripheral edema in highly malignant tumors. It is also useful to use MRI in delineating the response to treatment by radiotherapy or chemotherapy by documenting reduction in tumoral mass and restoration of normal MRI signals [15].

Despite increasing sophistication of radiological investigations, the radiologist is at best usually only able to offer a differential diagnosis. Osteosarcoma, for example, may be confused with stress fracture, chronic osteomyelitis, ectopic ossification, and other highly malignant tumors that may

induce active bone formation such as Ewing's sarcoma. Although the above radiological techniques are usually all that are required in investigation, new techniques such as dynamic MRI, whole body MRI and PET scanning are becoming more prominent and may be useful. Ultimately, however, the diagnosis rests in the hands of the histopathologist and analysis of biopsy material.

## Biopsy

Biopsy is the last but perhaps the most critical step in the evaluation of a bone tumor and should only be performed after extremely careful planning [16]. The surgeon who is responsible for the management of the patient with a primary bone tumor should be the individual to decide on the biopsy method and its approach. In a large series of patients with bone tumors, Mankin et al. [17] concluded that the incidence of significant problems in patient management resulting from inappropriate biopsy techniques was 20 % and that the incidence of wound healing complications related to a poorly planned biopsy was similarly high. They further noted that 8 % of biopsies produced a significantly adverse effect on the patient's prognosis and in 5 % led to an unnecessary amputation. Errors in diagnosis leading to inadequate treatment occurred twice as frequently when the initial biopsy was done at the referring hospital rather than a specialist center.

## Fine Needle Aspiration (FNA)

This technique, which is generally used in the diagnosis of soft tissue tumors, has also been popularized for initial diagnosis of primary bone tumors, particularly in Sweden [18]. A study of 300 consecutive patients not known to have a previous malignancy or suspected of having a local recurrence was analyzed. The FNA technique itself failed in 18 % of patients. In those patients where material was obtained, 95 % had correct diagnosis. It would appear that chondrosarcoma presented the greatest difficulty in diagnosis and Ewing's sarcoma the least. The only real advantage of FNA is that it can be performed under simple analgesia as an outpatient procedure. It is also worthy of note that FNA in benign bone lesions had a very high incidence of inconclusive results.

## Needle Biopsy

Targeted percutaneous needle biopsy using a Jamshidi or similar needle may often be sufficient to yield a diagnosis (Fig. 23.6). The technique is performed under radiological control and has 95 % accuracy when dealing with lesions of the appendicular skeleton [19]. In malignant lesions, the
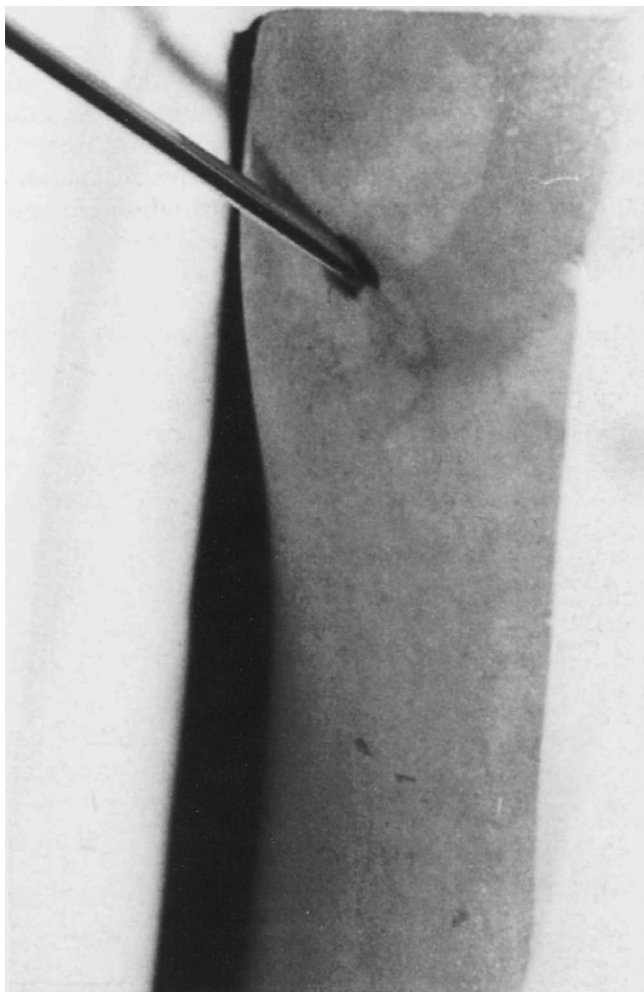
**Fig. 23.6** Targeted Jamshidi needle biopsy under radiographic control

needle biopsy tract should be subsequently removed en bloc with the tumor, and this requires a good rapport between surgeon and radiologist. Often, the tract can be marked with Indian ink following completion of the biopsy to facilitate removal. Failure to remove the tract may lead to local recurrence [20]. Although a rapid working diagnosis can often be achieved using frozen section or imprint techniques [21], it is important to emphasize that the analysis of small amounts of histological material requires pathological expertise of the highest caliber and is not, therefore, recommended if such expertise is not readily available.

## Incisional Biopsy

Most commonly, biopsy is performed by an open technique, and ideally the biopsy tract should be as small as possible and go directly to bone. Postoperative hemostasis at the operation site is mandatory, and the wound should be closed using a subcuticular suture. It must be remembered that when definitive surgery is performed, the complete biopsy tract and all contaminated tissue must be removed en bloc with the tumor. Failure to do so will significantly increase the risk of local recurrence [22]. The surgeon who performs the open biopsy should keep in mind the definitive procedure that may be required and place the biopsy site accordingly. There is no objection to the use of a tourniquet providing it is released prior to closure and hemostasis obtained. Drains may be used, but they should be brought out close to the wound and in line with it so that excision of the drain tract can also be obtained. There are advocates for closing the biopsy defect in the tumor pseudocapsule with cement, but there is no proof that this lessens contamination and may, if placed under pressure, theoretically further spread the tumor by the intramedullary route.

## Excisional Biopsy

Occasionally, an excisional biopsy will be more appropriate than either an incisional or needle biopsy. It is particularly indicated where the lesion is small and can easily be excised, often widely, without significant detriment to the patient's function. Lesions which are obviously applicable to excision biopsy are osteoid osteoma and osteochondroma, and it may also be appropriate in instances of low-grade chondrosarcoma affecting the medulla. It is often difficult to distinguish between active benign cartilage tumors and low-grade chondrosarcomas. When the entire lesion is removed allowing examination of the interface between the tumor, adjacent bone, and soft tissue, the pathologist is usually able to render a better opinion.

It cannot be overemphasized that in children osteomyelitis occurs more commonly than bone tumors. When in doubt material obtained, therefore, should also be sent for Gram staining and culture as well as histological analysis.

## Staging Notations

The correlation of information gained from radiological imaging investigations and the biopsy allows classification of a malignant bone tumor into a staging system. The surgical staging system proposed by Enneking et al. is easy to use clinically, and although it suffers from some significant oversimplification, it is generally acceptable [23]. The system is outlined in Table 23.2, and takes into account the three basic features that are recognized as having prognostic importance. These are, first, the histological grade of the tumor, second, its location and, third, the presence or absence of regional or distal metastases. The histological grade is classified as either low grade (G1) or high grade (G2). This grading system does not completely match purely histological grading systems but, in essence, low grade lesions will be the

**Table 23.2** Enneking's classification of surgical staging

| Stage | | Grade | Site | Metastases |
|---|---|---|---|---|
| I | A | Low (G1) | Intracompartmental (T1) | None (M0) |
| | B | Low (G1) | Extracompartmental (T2) | None (M0) |
| II | A | High (G2) | Intracompartmental (T1) | None (M0) |
| | B | High (G2) | Extracompartmental (T2) | None (M0) |
| III | A | Low (G1) | Intra- or extra- (T1–T2) | Regional or distant (M1) |
| | B | High (G2) | Intra- or extra- (T1–T2) | Regional or distant (M1) |

equivalent of Broders grade I and some II. The high-grade lesions would all be Broders II, III, and IV [24]. Regarding location, lesions are divided into those occurring in a specific compartment (T1) and those that are extracompartmental in nature (T2). The term "compartments" is defined as an anatomical structure bounded by natural barriers to tumor extension. Thus, a whole bone is considered a compartment as is a functional muscle group bounded by major fascial septa. Tumors spreading beyond these compartments or involving neurovascular structures are classified as extracompartmental. Some anatomical locations such as the axilla, antecubital fossa, periclavicular region, and midhand, are considered extracompartmental ab initio. In the lower limb the popliteal fossa and midfoot are similar problematic areas.

In malignant tumors, metastases occur most frequently to the lungs and they may occasionally occur in bone but are rare in local lymph nodes. When multiple bony lesions are sometimes seen, they are considered examples of multicentric primary tumors, though usually one lesion has the radiological features of a primary lesion and the others have characteristics of secondary intramedullary deposits. Skip lesions of an isolated area of tumor in the same bone as the primary were previously thought to occur in approximately 25 % of cases; more recent data suggests the true incidence is probably much lower [25].

Similar staging systems have been applied to benign disease, but unfortunately they rarely predict the clinical course of the problem. The most predictive element in the course of treatment of benign disease is, in fact, the surgical treatment which is given. For example, wide simple excision of a cartilaginous exostosis will lead to resolution of the problem providing that the cartilage cap is not broken, whereas curettage of a giant cell tumor may result in a local recurrence rate of approximately 20 %. In the upper limb, giant cell tumor commonly affects the distal radius and proximal humerus but tends to occur in only the mature skeleton. On the basis of the radiological appearance, Campanacci et al. [26] proposed four subtypes which redefine the previously proposed terms of latent, active, and aggressive. Unfortunately, grade I often represents a benign fibrous histiocytoma and the other grades do not necessarily predict their clinical behavior. The picture is further complicated by the histological pattern of the tumor.

The osteoclasts which are present are now considered to be only markers of the tumor activity, the tumor itself being represented by the stromal background. This background can vary from being very inconspicuous to frankly malignant [27]. This appearance can, of course, profoundly affect the extent of treatment. Primary de novo malignant giant cell tumor is a rare but well-recognized entity. Care is required, particularly in the differentiation of an osteoclastrich osteosarcoma. When diagnosed, the treatment of a malignant giant cell tumor is similar to managing a malignant fibrous tumor.

## Treatment of Common Primary Bone Tumors

### Benign Bone-Forming Tumors

#### Osteoma
These usually present as small, painless, slowly enlarging lumps. Although most commonly occurring around the skull, any bone may be affected. The radio logical appearance of an osteoma is a dense well-circumscribed lesion. Treatment is by surgical excision if the patient is symptomatic.

#### Osteoid Osteoma
This condition usually presents with vague pain, often nocturnal, and relieved characteristically by aspirin and other non-steroidal anti-inflammatory agents [28]. The pain may be associated with tenderness and vaso motor disturbance. Classically, the osteoblastic nidus is within the cortex or spongiosa of long bones. The nidus is less than 1 mm in diameter and induces intense surrounding reactive change (Fig. 23.7). If the nidus is in a subarticular location diagnosis can be difficult, as the reactive changes may not occur. Intracapsular osteoid osteomas around the elbow have been mistaken for tuberculous synovitis [29] and rheumatoid



**Fig. 23.7** CT radiograph of osteoid osteoma of the femur

arthritis [30]. It is also well recognized that longstanding disease can induce degenerative change [31].

The radiological investigation consists initially of a plain radiograph. This may or may not reveal the characteristic nidus. When marked reactive bone is seen, the differential diagnosis includes bone abscess, sclerosing osteomyelitis of Garré, osteochondritis, and stress fracture [32]. Bone scintigraphy will usually help localize a nidus but is relatively nonspecific. Computed tomography, if applied in close 2 mm sections, will be successful in identifying accurate locations of the nidus prior to surgical resection [33].

The treatment of osteoid osteoma requires excision or ablation of the nidus. As the nidus is surrounded by dense reactive bone this can be difficult to achieve. The traditional approach requires wide exposure with radiological verification of the site. Szypryt et al. [34] have described the use of intraoperative scintigraphy but this is rarely required. Excisional biopsy of the nidus under CT guidance is now performed with success [35] while electrothermal coagulation has also been explored and reported as successful.

The use of radioablation techniques has now become first-line management for the majority of osteoid osteomas, but it can be difficult in some sites, such as adjacent to the spinal column or in the very small epiphyseal areas of bones. Reported rates are of 90 % success with one treatment of radioablation. Five percent of cases require a second attempt at treatment by this technique. Only 5 % require surgical exploration and excision [36].

## Osteoblastoma

This lesion has a similar appearance histologically to osteoid osteoma, but is larger and does not induce as much reactive surrounding change. It is an extremely rare lesion affecting mainly the axial skeleton, although any bone may be affected. Patients are predominantly male in their second or third decades [37].

The clinical presentation is of vague pain, less severe than osteoid osteoma, and not particularly relieved by salicylates. Occasionally there may be both swelling and joint dysfunction.

The radiological features classically show an expansile radiolucent lesion, with a thin shell of peripheral new bone.

Treatment consists of either curettage with or without bone grafting or local excision. Local excision results in good local control but reconstruction may be required. This recurrence rate may be as high as 20 % following curettage, but the use of radiotherapy in extraspinal cases is rarely required [38].

## Malignant Bone-Forming Tumors

## Osteosarcoma

Osteosarcoma is the most common primary malignant bone tumor and can occur at any age, although most cases occur in the first two decades of life [39]. Most commonly affecting the two metaphyseal areas around the knee, the humerus is the third most common site, with tumors often arising at an earlier age than in the lower limb [40].

Osteosarcomas are usually subtyped on the basis of their histological patterns as fibroblastic, chondroblastic, osteoblastic, telangiectatic, or mixed [41]. Although the subtype classification was originally thought to have a bearing on prognosis, carefully controlled studies now suggest that this is not the case. Histological grading is also an unreliable prognostic indication [42].

Patients present usually with a short history of pain followed by swelling, joint dysfunction, and occasionally pathological fracture. The many radiological advances which have occurred in the last decade have allowed very accurate staging of the tumor. The plain radiograph remains the initial diagnostic tool but tends to underestimate the local extent of the tumor. Accurate visualization of cortical destruction and soft tissue spread will be given by CT but this may miss skip lesions in the same bone. It is a useful technique in planning biopsy and local excision [43]. Today, CT of the chest is the accepted staging investigation to assess the potential presence of pulmonary metastases. Local staging of disease now depends heavily on MRI studies, particularly in the T2 mode, which will delineate accurately the intramedullary and soft tissue extent of the lesion; MRI will outline the relationship of the tumor to the adjacent joints and blood vessels (Fig. 23.8).

Preoperative bone scintigraphy using technetium isotopes is useful in identifying skip lesions and metachronous lesions in other bones. The radioisotope scan may also on occasions demonstrate pulmonary metastases [44].
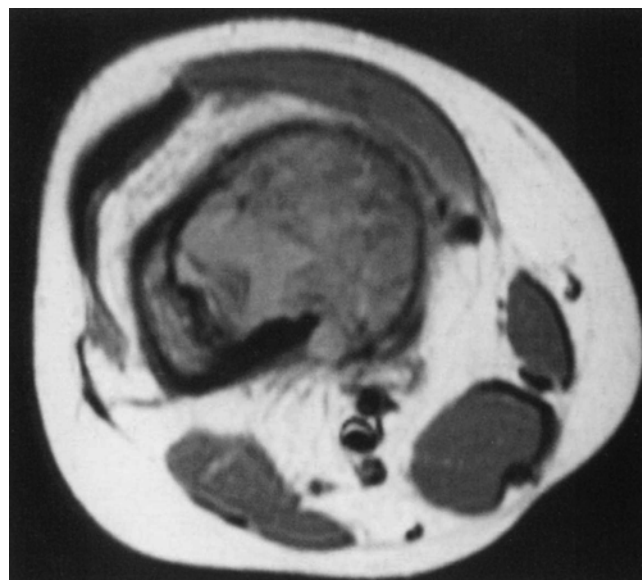


**Fig. 23.8** MRI which outlines the relationship of the tumor to the adjacent joints and blood vessels

Having performed the radiological staging procedures, it is necessary to establish the pathological diagnosis. At this stage a biopsy is performed. Many argue that an open biopsy is required. However, Stoker et al. [19] have shown the accuracy of Jamshidi needle biopsy cores obtained in a referral center under local anesthesia and image intensification. More recently similar accuracy has been shown in biopsying the soft tissue component of malignant tumors under ultra sound or MRI [45].

Historically, the early treatment of osteosarcoma was surgical ablation. In the upper limb this required either disarticulation of the shoulder for lesions in the distal humerus or forequarter amputation for more proximal growths. Survival, however, was poor with 5 year survival rates varying between 11 and 25 % [46]. Cade [47] reported an alternative method of treatment employing preoperative radiation followed by surgical ablation only in those cases not developing pulmonary metastases. Many less amputations were performed but the survival rate was unaltered. This was subsequently confirmed by other series [48].

By the early 1970s, it became evident that this appalling survival rate might be improved by the use of adjuvant chemotherapy. Many different protocols were developed, some claiming a very high survival rate [49], but controlled trials of therapies were not performed. In the UK, the Medical Research Council combined with the European Organization for Research into Cancer Treatment (EORTC) set up controlled trials of adjuvant chemotherapy. More recently neoadjuvant chemotherapy has been employed and allows treatment of undetected micrometatases and causes necrosis of the tumor and may allow some shrinkage of the primary tumor. This latter effect may allow easier local resection and reconstruction of the limb. The initial trials compared the effect of Adriamycin (doxorubicin) and cisplatin with or without high-dose methotrexate. The two-drug arm performed better, resulting in a survival rate of 65 % at 5 years. This two-drug arm has been compared with a Rosen T10 regime. The trial has accrued 400 cases. Analysis of them showed no material difference between the two regimes, therefore the two-drug regime is preferred because of less morbidity. A second trial attempting a dose intensification of the two-drug regime, the three courses of chemotherapy being given over 6 weeks as opposed to nine, using rescue by granulocyte cell stimulating factor, has also shown little difference in outcome. A further regime is now in progress which hopes to improve the cure rates of osteosarcoma. The trial is worldwide, involving both European and American oncologists and hopes to improve the outcomes which have been somewhat disappointing over the past 20 years. This randomized trial termed Euramos hopes to herald a new era of clinical investigation into osteosarcoma, which of course should always be treated under the guidance of a specialist team [50].

Surgical intervention is now performed at around the tenth or eleventh week following commencement of chemo-therapy and is continued in a randomized manner in the postoperative period. In most cases, a "wide excision" of the tumor is performed outside the tumor pseudocapsule with preservation of the neurovascular bundles, although often in tumors arising in the upper limb the circumflex nerve and the radial nerve may often be sacrificed to allow adequate clearance. Following wide excision functional reconstruction is only possible using either customized endoprostheses or allografts. A recent multi-central pan-European trial has found no significant improvement in either local recurrence or survival in cases treated by chemotherapy.

## Parosteal Osteosarcoma

This is a low-grade malignant tumor developing on the external surface of large bones. The disease was first reported by Geschickter and Copeland in 1951 [51]. It has a long natural history and tends to affect patients in the second and third decades of life. Most patients present with a longstanding swelling associated with dull ache. The elbow is only rarely affected.

Treatment consists of wide local resection of the tumor with appropriate reconstruction. It is generally accepted that in most cases chemotherapy is not indicated. Review of the tumor may show high-grade changes in the fibrous elements. These tumors have a poorer prognosis [52], and adjuvant chemotherapy may be indicated. Occasionally, the low-grade component may transform or dedifferentiate to a high-grade osteosarcoma [53]. Treatment for these latter cases is then as for an osteosarcoma (see Chap. 18).

## Periosteal Osteosarcoma

This is a very rare tumor; many still doubt its existence, although it probably is a variant of parosteal osteosarcoma with a prominent cartilaginous component [54, 55]. These tumors are usually small unicortical lesions (Fig. 23.9). Treatment is by wide resection and reconstruction where required. Whether chemotherapy is required in their management is still unclear [56].

## Benign Cartilage-Forming Tumors

### Osteochondroma

These cartilage-capped bony protrusions may develop in any bone derived from cartilage. They are usually discovered in childhood and many are found only as incidental findings on radiography (Fig. 23.10a, b). They are usually painless but pain can be invoked by mechanical irritation or nerve compression. Pseudo aneurysm has also been reported specifically in the popliteal regions [57].

If symptomatic, straightforward excision at the base is curative. If asymptomatic, they can be safely observed. Growth will continue until skeletal maturity. If growth appears to occur after skeletal maturity then malignant transformation must be considered even if the radiographic appearances do

not alter. It is now considered that the size and thickness of the cartilage cap as assessed by MRI or CT is the critical factor. This is of course not visible on plain radiographs.



**Fig. 23.9** Periosteal osteosarcoma of the tibia

In diaphyseal aclasis the patient may also present with growth abnormality and subluxation of joints. Removal of the lesions is rarely enough and the patients often require major reconstructions to correct the deformities [58]. The patient should be warned specifically of the possibility of malignant change associated with growth after maturity. Known lesions which cannot be palpated should be monitored by radiography. Unfortunately, bone isotope scanning cannot reliably differentiate benign from malignant cartilage lesions, but recent innovations such as PET scanning may be helpful in this regard [59].

## Chondroblastoma

This is a rare bone tumor usually located in the epiphyseal plate which is essentially benign. Jaffe and Lichtenstein consider that it is a tumor developed from cartilaginous germ cells, although Higaki considers the cell of origin to be histiocytic [60, 61]. Typically, the patient is in the second decade and is more likely to be male. A long prodromal history is typical and there may be muscle wasting and restriction of joint movement [62]. The most common site of occurrence is the upper humeral epiphyseal plate, although they can be associated with any primary or secondary site of ossification.

Typically, the lesion is radiolucent crossing the growth plate and intralesional calcification can be seen particularly with CT [63] (Fig. 23.10). CT may better illustrate the local invasive properties of the tumor. It is well recognized that chrondroblastoma may be associated with secondary implantations in the lung. These "areas" if resected have a "benign" histological appearance and therefore represent implantation of vascularly transported tumor tissue rather than true metastases.
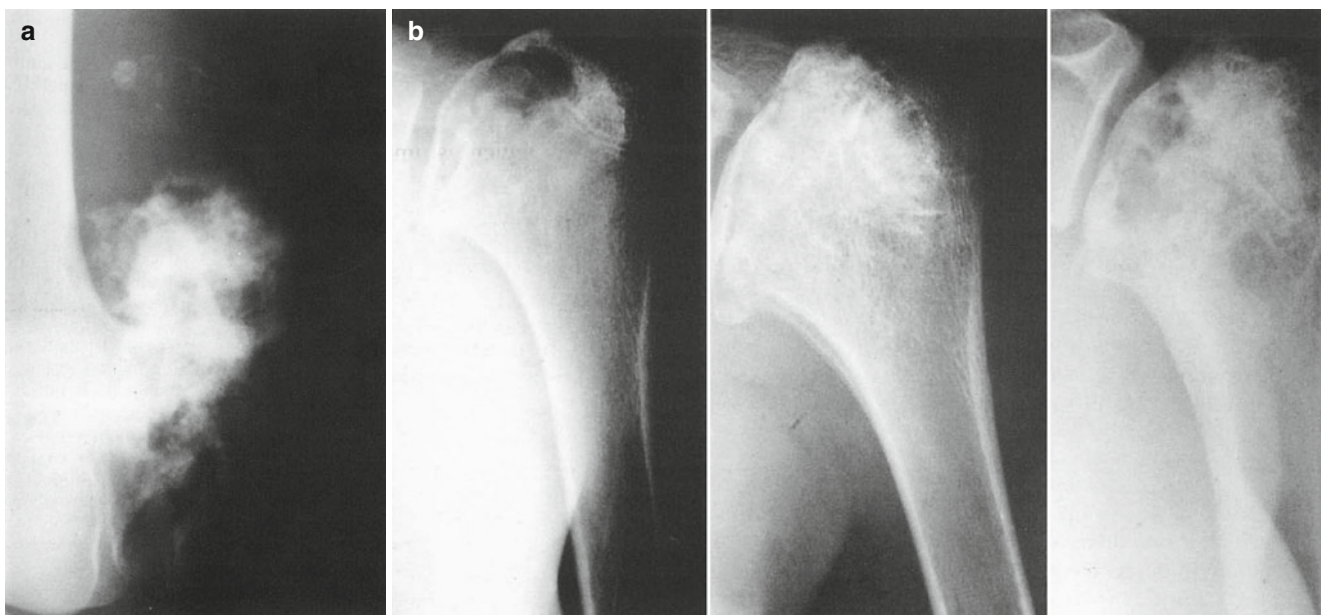


**Fig. 23.10** (**a**) Lateral radiograph showing osteochondroma of distal femur. (**b**) AP radiograph of proximal humerus showing chondroblastoma

**Fig. 23.11** AP radiograph of distal femur showing a chondrosarcoma arising in a pre-existing enchondroma

Treatment of the local lesion is by a combination of curettage and excision of any adjacent soft tissue extension. The outcome is very good but it may recur if not excised totally, and damage may be done to the growth plate. The application of autologous bone graft will lessen the recurrence rate but conversely makes local recurrence more difficult to detect by radiography. The recurrence rate is approximately 20 %, but this may be further reduced by use of cryotherapy and other adjuvants [64].

### Chrondromyxoid Fibroma

This is a tumor which arises commonly in the upper tibia. It is most common in the second decade of life but may occur in any decade. There is a long prodromal history, often as long as 2 years [65]. With the exception of the clavicle, all bones can be involved, but it is much more common in the lower limb.

The radiological features are of an eccentric lesion in the metaphyseal area of a long bone. It is well de fined but surrounding sub-periosteal reaction may be slight [66].

As with chondroblastoma, treatment consists of an initial curettage and the recurrence rate can be reduced if the operation is supplemented with an autograft [67].

## Malignant Cartilage-Forming Tumors

### Chondrosarcoma

Chondrosarcoma is divided into two basic subgroups: primary chondrosarcoma which arises in normal bone, and secondary chondrosarcoma which arises in a pre-existing benign cartilage tumor, usually an enchondroma or cartilage cap of an exostosis. Primary lesions are twice as common. Chondrosarcoma occurs in 25–30 % of cases, secondary to enchondroma or an exostosis. Primary chondrosarcoma rarely occurs in childhood.

Although chondrosarcomas may occur in the young, they predominate after the third decade of life. Both sexes are equally afflicted. Most patients complain of pain but it is well recognized that a presenting mass may be painless [68]. The anatomical distribution favors the axial skeleton, but 10 % of tumors occur in the humerus.

Classically, the radiological appearance is a thick walled radiolucency with irregularly blotchy areas of calcification. On the medullary surfaces the cortex is scalloped and cortical penetration occurs late in the disease. A pre-existing benign tumour (Fig. 23.11) may be difficult to discern.

The only treatment effective in chondrosarcoma is excision, the adequacy of which is important in determining the outcome [69]. The survival outcome is also influenced by the degree of malignancy and the site, patients with pelvic lesions faring far worse than those with upper limb tumor. Although most lesions require excision, preferably of a wide or radical nature, small corticated, low-grade lesions in the elderly may be best served by curettage and adjuvant therapy consisting of cryosurgery, phenolization or "cement" application.

### Dedifferentiated Chondrosarcoma

This rare tumor was first described by Dahlin and Be about in 1971 [70]. Additional mesenchymal elements are present in addition to the chondrosarcoma. The humerus is the second most common site. The radio logical appearance may give a clue to the probability of this lesion, which may be represented by a purely lytic expansile area in an otherwise typical chondrosarcoma. The overall poor prognosis of patients with this tumor has led to attempts with the use of chemotherapy as a neoadjuvant therapy in addition to surgery, with little success.

### Mesenchymal Chondrosarcoma

This is a further subtype of chondrosarcoma which rarely affects the upper limb. It is characterized by a highly cellular

primitive spindle cell stroma with focal chondroid differentiation [71]. The tumor occurs most frequently in the second decade of life.

In terms of radiography, it is extremely difficult to differentiate the lesion, which may resemble an osteosarcoma as soft tissue extension may be heavily calcified.

Treatment is similar to dedifferentiated chondrosarcoma, consisting of chemotherapy and resection. In Britain, the chemotherapy consists of the agents cisplatin, ifosfamide, and Adriamycin (doxorubicin).

## Clear Cell Chondrosarcoma

This is an extremely rare tumor which is rather slow growing, patients often having symptoms for up to 3 years. The most common site is the upper femur but the upper limb may also be affected [72]. The tumor appears as an osteolytic expansile lesion, usually at the proximal end of long bones. Treatment consists of complete surgical excision with reconstruction.

## Benign Tumors of Histiocytic or Fibrohistiocytic Origin

### Giant Cell Tumor

This is a locally aggressive but essentially benign bone tumor. It accounts for 5 % of all primary bone tumors and afflicts the mature skeleton. There is a slight female predominance [73]. Although commonly affecting the knee, distal radius, and proximal humerus, the elbow region may be affected (Fig. 23.12) and indeed patients with multiple sites have been recorded [74]. All patients suspected of presenting with a giant cell tumor should have hyperparathyroidism excluded by biochemical testing.

Early lesions present radiographically as an expanding lytic lesion, eccentric to the long axis, often with fine trabeculae present. Most investigators believe that the tumor arises in the epiphysis (subarticular region) and extends to involve the metaphysis. Large lesions progress to cortical destruction and joint dysfunction.

On the basis of the radiological appearance, Campanacci et al. [26] have proposed four subtypes which redefine the previously proposed terms of latent, active, and aggressive. Unfortunately, grade I probably often represents benign fibrous histiocytoma and the other grades do not necessarily predict their clinical behavior. The picture is further complicated by the histological pattern of the tumor. The osteoclasts which are present are now considered markers of the true tumor which is represented by the stromal background. This background can vary from being inconspicuous to frankly malignant [27] and thus can profoundly affect treatment.

Another poorly understood phenomenon in these tumors is the likelihood of malignant transformation of a benign



**Fig. 23.12** Giant cell tumor: lateral x-ray of elbow joint

tumor either following multiple local recurrences or irradiation treatment [75], and care is required in establishing whether it is true malignant transformation of the giant cell tumor or sarcomatous induction by the radiotherapy when this modality of treatment has been used.

Primary de novo malignant giant cell tumor is a rare but well recognized entity, but care is required particularly in the subsequent differentiation of an osteoclast rich osteosarcoma [76]. When diagnosed, their treatment is as for a malignant fibrous tumor (see below).

Given the multiplicity of combinations of local extent and histological appearance, it is difficult to be adamant regarding therapy. It is well recognized that curettage alone has a 20 % or greater local recurrence rate [77]. Recent work by the European Musculoskeletal Oncology Society in a multicenter study suggests that the incidence of recurrence might be halved if adjuvant therapy (phenolization, cryotherapy, or polymethylmethacrylate) is used in combination with intralesional techniques.

Curettage remains the mainstay of treatment; occasionally multiple attempts may be required. Reconstruction may

not always be required after curettage and a number of patients have been treated by simple casting or cast-bracing until infilling of the cavity [78]. If articular failure has occurred by fracture or tumor invasion, then reconstruction with a pros thesis or allograft will be required.

### Non-ossifying Fibroma/Benign Fibrous Histiocytoma

Non-ossifying fibroma is generally the term given to a lesion which is larger than a fibrous cortical defect. The term metaphyseal fibrous defect may be used for both. The lesions are extremely common between the ages of 4 and 8 years and can affect any metaphysis [79]. They are rarely seen in adults, which probably reflects the natural history of the condition. Large lesions may be associated with pathological fractures [80].

The radiological features are characteristic, consisting of an eccentric lesion which may involve the cortex situated at the end of the diaphysis. A sclerotic rim is usually seen on the medullary border. Although the lesion does not usually require biopsy, unusual clinical or radiological features may justify the need for needle biopsy.

Treatment in the majority of cases is only observation. Enlargement or pathological fracture will demand curettage or block excision with or without bone grafting. Fractures occasionally lead to obliteration of the lesion [81].

Benign fibrous histiocytoma may have a similar histological picture to a non-ossifying fibroma but tends to occur in older patients and is sited away from the metaphysis. Treatment requires either curettage or block excision.

### Malignant Tumors of Histiocytic or Fibrohistiocytic Origin

#### Malignant Fibrous Histiocytoma

Malignant fibrous histiocytoma was first described by Feldman and Norman in 1972 [82]. It is a high-grade spindle cell lesion of bone which accounts for approximately 5 % of all bone tumors. Although the peak incidence is in the fifth decade, it may occur at any age. Females seem to be preferentially affected in the second decade. Histologically, it resembles its soft tissue counterpart but must be differentiated from this and from fibroblastic subtype of osteosarcoma. The latter may be differentiated by osteoid or alkaline phosphatase production [83]. The clinical presentation is as for other bone tumors, with a usually fairly lengthy duration. The area affected is usually around the knee and the radiographic features are of a tumor with essentially a lytic component with ill-defined margins. Lymph node metastases may occur [84]. Unlike its soft tissue counterpart, malignant fibrous histiocytoma of bone has been shown to respond well to a number of chemo-

therapeutic agents, including Adriamycin (doxorubicin), ifosfamide, high-dose methotrexate, and cisplatin. Therefore, a combined approach using adjuvant or neoadjuvant chemotherapy, together with adequate surgery, seems the treatment of choice.

### Bone Tumors of Vascular Origin

#### Hemangioendothelioma

Hemangioendothelioma is a locally aggressive nonmetastasizing tumor. All age groups can be affected and there is a male predilection. Radiographic appearances are of an osteolytic lesion which may occasionally produce a honeycomb pattern. Treatment is by adequate local surgery. Local recurrence is a problem.

#### Hemangiopericytoma

This is a low-grade malignant spindle cell tumor rep resenting 0.1 % of malignant bone tumors. It is also more common in males [85]. It again resembles its soft tissue counterpart and presents as an osteolytic bony lesion. The pelvis and lower limbs are more commonly affected. Wide surgical excision is the treatment of choice. The role of chemotherapy or radiotherapy is not yet established. Unfortunately, local recurrence is extremely common and metastases may occur extremely late.

#### Angiosarcoma

This is the high-grade counterpart of hemangioendothelioma. It is exceedingly rare. Again, wide surgery is the treatment of choice. Vascularity of the tumor may make limb salvage surgery extremely difficult. The tumor is radiosensitive [86]. The role for chemotherapy is not yet established.

### Adamantinoma

Adamantinoma is an extremely rare bone tumor which occurs commonly in females, mainly in the second decade of life (Fig. 23.13). The bone which is commonly affected is the tibia [87]. Histologically, there is a mixture of spindle cells forming a fibrous stroma and islands of epithelial-like cells. It often arises in a background of fibrous dysplasia, and a differential diagnosis from metastatic carcinoma in the older patient may be difficult because of the expression of epithelial markers. Occasionally, other long bones can be affected and multi-focality has been recorded. Diagnosis may take many years because of the slow growth of the tumor. Radiologically, the lesion is lytic and well defined. Metastases are only found late in the disease. Treatment is excision, usually involving limb-saving techniques applied after diaphyseal resection and re construction.

**Fig. 23.13** AP and lateral view of adamantinoma of the tibia



**Fig. 23.14** Ewing's sarcoma of the femur exhibiting typical periosteal lamination (onion-skinning)

## Ewing's Sarcoma

Ewing's sarcoma is the second most common malignant bone tumor of children and adolescents. Although there is a wide histological spectrum, 10–15 % of tumors fall into the category of malignant round blue cell tumor/Ewing's sarcoma [88]. The mean annual incidence approximates 0.6 per million of the total population [89]. It is rare below the age of 5 years, and the peak incidence is between 10 and 15 years. Male to female ratio is approximately 1.5:1, but this may vary with the age of the patient. Black and Chinese populations are less affected [90]. In addition to the standard presenting features, fever may occur, and this is more likely in patients with advanced or metastatic disease [91]. Pelvis, femur, tibia, and fibula account for 60 % of all primary sites. Although the plain radiographic appearance may be characteristic with a moth-eaten central bony destruction having poorly defined margins and an associated parallel onion-skin periosteal lamination together with a large soft tissue extension, this picture is not always seen (Fig. 23.14). Further investigations are required to

confirm the diagnosis. Approximately 20 % of patients present with detectable metastases [92] which may be either pulmonary or be represented by multiple bone/bone marrow involvement. The serum lactate dehydrogenase (LDH) level may be elevated and this is associated with a poor prognostic outcome [93]. Other factors having a favorable influence on prognosis in Ewing's sarcoma are female gender [94], tumor volume at presentation [95], histological type [96], and proven histological response to chemotherapy [97].

Ewing's sarcoma represents a tumor where the utmost collaboration is required between surgeon, radiologist and pathologist. The radiological appearance of osteomyelitis may be very similar, and this can be further complicated if the patient has a leucocytosis and/or fever. The pathologist must differentiate Ewing's tumor from primitive neuroectodermal tumor (PNET) and Askin's tumor, which can be done using neural specific immunohistochemistry. Similar problems may occur in distinguishing the tumor on histological grounds from rhabdomyosarcoma, neuroblastoma lymphoma, and

small cell osteosarcoma. Rarely, primary malignant lymphoma of bone can present without disseminated lymph node or visceral disease. Again, immunohistochemistry using lymphoid markers is helpful in recognizing this category of tumor [98]. Ewing's sarcoma may also present as a extraskeletal lesion without a perceptible bony component. In this variant, there is a higher risk of lymphatic spread; this rare variant is usually treated using the principles employed in embryonal rhabdomyosarcoma [99]. There is no doubt that Ewing's sarcoma is a rapidly disseminating malignancy. Prior to the advent of effective chemotherapy, 90 % of patients died within 5 years. Conventionally, radiotherapy has had a major role in local treatment in Ewing's sarcoma [100]. Although the risk of local failure following radiation alone is difficult to assess, there is increasing evidence that the probability of cure with radiotherapy is related to limited tumor bulk and chemosensitivity as measured by tumor regression [101]. Radiotherapy also can affect growth if the epiphyses are treated leading to limb deformity and length inequality, and radiotherapy around the joints may lead to contracture formation. Radiotherapy in the pelvis may lead to visceral or gonadal damage, although excision alone may be similarly fraught with morbidity [102]. Although the debate continues, it is generally recognized that operative intervention is indicated for the local treatment in Ewing's sarcoma. In the axial skeleton, surgery is rarely indicated but in the pelvis considerable problems may be posed. Certainly, pelvic tumors are usually large and have extensive soft tissue extension invading the pelvic cavity when initially diagnosed. Their prognosis is particularly poor [103]. There is now good evidence that the prognosis of extensive pelvic lesion can be improved when the residual interosseous disease (following chemotherapy) is resected and reconstruction performed. Such resections are rarely "wide" and therefore are usually followed by postoperative radiotherapy. Whether radiotherapy can be omitted in patients who have had a particularly good chemotherapeutic response is the subject of ongoing controlled trials [104]. (For management of Ewing's tumor affecting the chest wall see Chap. 18.)

### Simple Bone Cyst (Unicameral Bone Cyst)

These fluid-filled cysts often arise in the metaphyseal region of long bones juxtaposed to the epiphyseal plate. They are usually brought to the patient's attention either by incidental Xray or by pathological fracture. Fracture may lead to resolution of the cyst, but it is also well recognized that a traumatic episode may turn a cystic lesion into an aneurysmal bone cyst [105].

Cysts are commonly found in the proximal humerus and femur but may also occur in both the radius and ulna. They are commonly seen in childhood and adolescence, 90 % of patients being younger than 20 years old. When they do occur in the adult, they tend to occur in either the ilium or os calcis.

Plain radiographs usually show a lesion which has a central medullary location and its length is usually greater than its width (Fig. 23.15). The transverse diameter of the cyst closest to the epiphysis is recognized as being as wide as the epiphysis. With age, the cyst grows towards the diaphysis. This appearance is contrary to an aneurysmal bone cyst (see below), which shows a centrifugal growth pattern. Where the cyst reacts with cancellous bone there is a bony reaction but periosteal reaction is extremely rare. There is no soft tissue component. Further radiological investigation is rarely performed, although it is possible to recognize fluid levels on a CT scan. Treatment can be difficult. Small cysts which are asymptomatic do not require any therapy. However, large cysts may require curettage, bone grafting, en bloc resection, or even nailing. It is now fairly universally accepted following the work of Campanacci et al. [106] that these cysts will respond to an injection of methylprednisolone. If surgery is contemplated, incomplete removal of the cyst lining usually leads to local recurrence. The recurrence rate is much higher in children [107].

### Aneurysmal Bone Cyst

These blood-filled expansile lesions present with pain and swelling and may follow a fracture. It is recognized that during pregnancy aneurysmal bone cysts may rapidly enlarge.

It is predominantly a disease of the first three decades of life and occurs equally in both sexes. It can affect any bone and 80 % are recorded as occurring in the upper limb.

The radiological features are of a purely lytic expansile lesion which usually arises in the metaphysis. Extension may occur into the epiphysis when the growth plate has closed [108]. They may grow alarmingly and may mimic malignant tumors (Fig. 23.16). Again, if further radiological investigation is required, the multiple fluid levels seen on CT are practically diagnostic of an aneurysmal bone cyst [109].



**Fig. 23.15** Simple bone cyst proximal femur

**Fig. 23.16** Aneurysmal bone cyst proximal fibula showing large bone expansion

The mainstay of treatment is a combination of curettage and bone grafting. Where the tumor arises in inaccessible sites or where excessive blood loss is feared, arterial embolization may be a helpful adjunct to treatment. In tumors that recur or remain inaccessible, small doses of radiation can be given [110].

## Miscellaneous Tumors of Soft Tissue and Bone

### Myositis Ossificans

This condition is particularly troublesome when it occurs around the elbow joint. Although it can occur following a single injury, it more usually follows chronic repetitive trauma. The most usual presentation is of a painless mass, although some patients may have considerable soft tissue inflammation and pain. The period of symptoms is usually short.

The radiographic features show no abnormality in the first 2–3 weeks and then speckled calcification becomes evident.

A fully mature lesion can usually be seen at around 14 weeks. In general, the diagnosis should be made on clinical and radiological grounds as great care is required in the examination of a biopsy. Unfortunately, myositis ossificans can be easily mistaken for osteogenic sarcoma [111].

Treatment is usually by surgical excision, but this should not be performed until the lesions have matured. Surgical intervention prior to maturity leads to a high rate of local recurrence.

## Surgical Management

### Embolization

Though angiography is now rarely used in pre-surgical imaging protocols, it can be useful in helping the clinician decide whether a plane of dissection exists between the tumor and the local neurovascular structures and, therefore, allow some limb salvage procedure to be performed. Occasionally, in tumors such as aneurysmal bone cysts, hemangiomas, and vascular osteosarcomas, such as the telangiectatic variety, significant feeding vessels can be recognized. Use of embolization materials injected into these vessels may significantly decrease the vascularity and render excision either possible or more easily accomplished. Embolization may be accompanied by significant pain and discomfort in the affected limb and the procedure should really be timed to allow for surgery to follow within 24 h. Embolization used solely as a method of local treatment is not recommended.

### Curettage Alone

Certain benign tumors, notably aneurysmal bone cyst and giant cell tumor, lend themselves to treatment by intralesional removal or curettage. The technique of curettage requires a direct approach to the most weakened part of the cortical bone in expansile lesions or the most anatomically easy access in true intramedullary lesions. A good window of cortical bone is removed to allow adequate visual access to all the various crevices within the medullary cavity. A thorough curettage is performed with a standard bone curette and the cavity is then further debrided using either an osteotome or dental burr. The whole cavity is then thoroughly lavaged with a pressurized pulsed lavage system. Giant cell tumor local recurrence rate as high as 40 % can be recorded with this technique alone. Most surgeons now prefer to add some form of adjuvant therapy; the use of adjuvant therapy will decrease the local rate of recurrence to less than 15 %. Local adjuvants which have been proposed include cryotherapy, phenolization, and the use of cement, the latter having a dual role; first, the hyperthermic

reaction produced in the setting of cement causes local necrosis and further decreases the local recurrence rate, and, second, the cement itself may give immediate structural strength. For the younger patient, most authors prefer to remove the cement after an interval and substitute with bone graft. Lesions sited in the proximal humerus or distal radius are more suited to the simple curettage technique (Fig. 23.17).

## Curettage and Bone Graft

When benign tumors occur in the subarticular position, the sub-chondral bone can be eroded and deformity of the articular surface can be encountered (Fig. 23.18). Treatment, therefore, must consist of gaining some mechanical support with either fresh autograft or allograft. The lesion is curettaged in the above manner and then morsellized cancellous auto graft harvested from the iliac crest is inserted into the defect. This will allow reconstitution of the subchondral space and support the articular architecture of the joint (Fig. 23.19). Bone autograft is incorporated relatively quickly. The exact mechanism by which this incorporation occurs is not fully understood but has been previously investigated and reported by Burwell [112]. The initial phase of incorporation in the first 2 weeks is analogous to fracture healing and is equally effective on both cancellous and cortical bone. Osteoblasts are laid down on the surface of the graft, and in the case of cancellous bone the osteoid seen laid down on top of the transplanted trabeculae of bone are rapidly absorbed. Eventually, all the graft of cancellous nature is resorbed. Where cortical fragments exist, the revascularization rate is slower and cortical fragments may be retained even following long-term incorporation. For this reason, cancellous grafting is preferred unless some mechanical strength is required, when cortical or fibular struts may be preferred. In recent years increasing use of bone graft substitute such as ApaPore, a synthetic hydroxy-appetite, have gained increasing amounts of popularity. They obviously avoid the morbidity of donor site harvest and usually incorporate within 6 months.

## Excision Alone

Certain benign tumors which occur eccentrically on the bone surface are suitable for simple excision. The most classical variety is a osteochondroma or actively growing exostosis (Fig. 23.20). Here, surgical therapy merely requires resection of the bony stalk of the exostosis at the junction with the host bone. Care must be taken, however, not to spill any of the cartilage fragments, which may lead to local recurrence. The technique of local excision can also be



**Fig. 23.17** Giant cell tumor of distal radius



**Fig. 23.18** Giant cell tumor of distal radius showing deformity of the articular surface

extended to lesions such as non-ossifying fibroma, which occur eccentrically in the metaphysis of bone, and to certain low grade malignant tumors, such as periosteal osteosarcoma, where the resulting defect in the diaphysis may not be great. However, care must always be taken to achieve an

**Fig. 23.19** Lesion of distal radius following curettage and bone grafting

adequate surgical margin to prevent local recurrence, but most surgical oncologists now believe that the initially reported 5 cm margin is no longer required. Certainly, an adequate rim of normal host bone is all that is necessary, although occasionally this may require grafting techniques to reconstitute the diaphysis (Fig. 23.21).

## Osteoarticular Fibular Transplantation

This technique is suitable for fairly large defects which occur following resections of benign or aggressive tumors of the distal radius and proximal humerus. The proximal ipsilateral fibula is harvested and is generally used in a non-vascularized manner. Transplanted to the upper humerus, it will allow a rudimentary shoulder joint which is relatively pain-free, particularly in the younger child. There may also be some hypertrophy of the graft. When used to reconstitute the distal radius, the articular surface is placed adjacent to the scaphoid bone and acts as a structural support and articulation. The fibula is usually plated onto the residual radius and the radial collateral ligament of the wrist reconstituted by using a loop of extensor carpi radialis longus. An illustrative case is seen in Fig. 23.22.

## Bone Transportation

This technique originally described by Ilizarov [113], originally used in congenital deformity and post traumatic situa-



**Fig. 23.20** Preoperative Illustrations of a proximal humeral osteochondroma

tions, is now extended to the use of filling postsurgical defects following tumor surgery. The principle is to transport a bone cylinder over the length of the defect and achieve bony closure at the proximal end of the defect by callus distraction and at the distal end of the defect by contact of the cylinder with the host bone. It has significant problems in that it involves prolonged external fixation time of several months, although this is less so in the upper limb. All transport systems suffer from pin track infection and the incidence of this limits the technique to benign tumors. The technique is contraindicated, in my opinion, in malignant tumors where patients are undergoing chemotherapy. Extremely short defects can be managed by acute shortening of the limb followed by reconstitution of the length using a technique of callus distraction (Fig. 23.23). The regenerate bone is often difficult to visualize on plain radiography and the use of ultrasound techniques is indicated to measure the degree and quality of the bone regenerate. In the lower limb, rapid internal fixation and distal bone grafting is recommended, but in the upper limb this does not seem to be a problem. Simple stabilization of the lengthening, which allows the regenerate to mature, appears to be all that is required. The technique is limited to diaphyseal defects. The rate of distraction is usually 1 mm per day, often in four quarter turns of the distracting device [114].

**Fig. 23.21** Fibular grafting to
reconstitute the diaphysis
following tumor excision



## Surgery for Large Osteoarticular Defects

When considering whether limb salvage procedures are jus-
tified, it has been traditional to consider the long-term onco-
logical result and compare that with results obtained
historically with amputation. Subsequent comparisons can
be made in four broad areas:

1. Is there any difference in overall survival by patients
   treated by the two methods?
2. What is the early and late morbidity for each type of
   reconstruction?
3. Is the function of the salvaged limb satisfactory and does
   it remain so over a period of prolonged follow up?
4. Are there quality of life issues for patients undergoing
   limb salvage procedures as opposed to amputation?

## Overall Survival

There have been a number of reports from single institu-
tions [115, 116] which have concluded that the perfor-
mance of limb salvage operations had no effect on the

long-term survival of patients. These early reports have
been confirmed by a number of multi-institutional reports
[117–119]. Simon et al. point out that the local recurrence
rate of patients undergoing above-knee amputation for
malignant bone tumors around the knee is about 10 %,
which is not dissimilar to patients undergoing limb salvage
procedures. However, no patients who had a hip disarticu-
lation suffered a local recurrence although at the cost of
significant mutilation. Simon [120] reports a study from the
Musculoskeletal Tumor Society, where the development of
local recurrence was an extremely bad prognostic factor.
Sixteen of seventeen people who developed local recur-
rence following limb salvage or amputation eventually died
of their disease. Certainly, local recurrence usually requires
amputation if there is no other metastatic disease. Even fol-
lowing amputation it would appear that survival is still
unlikely. It is still, however, unclear whether the local
recurrence represents poor response of the tumor to neoad-
juvant chemotherapeutic agents and hence a poor prognosis
or whether it is merely poor surgical decision making.
There are, of course, a large number of cases, particularly
where local recurrence occurs late and is not associated
with metastatic disease, where further limb salvage proce-
dures may be considered.

**Fig. 23.22** Osteoarticular fibular transplantation of the distal radius in giant cell tumor



**Fig. 23.23** (**a**) Initial radiograph following bone transportation of the tibial diaphysis. (**b**) Final radiograph following bone transportation of the tibial diaphysis

## Early Complications

Operations performed for limb salvage are fraught with complications. Acute vascular injury may occasionally occur, and venous thrombosis and pulmonary embolism may be encountered in the early post-operative period. Involvement of neural structures often leads to sacrifice of a nerve during resection of the tumor, but the most worrying complication in the early postoperative period is wound necrosis and subsequent infection. Loss of cutaneous cover requires urgent soft tissue coverage, often by a local skin flap or rarely by a myocutaneous free flap, so that the method of reconstruction can be covered. If infection ensues, then the complications, particularly where an endoprosthesis has been used, may be devastating. Often the limb requires amputation in the short or medium term. The onset of infection also delays the planned return of the patient to adjuvant chemotherapy.

It is important to emphasize that amputation itself is not without short and long-term complications, and certainly
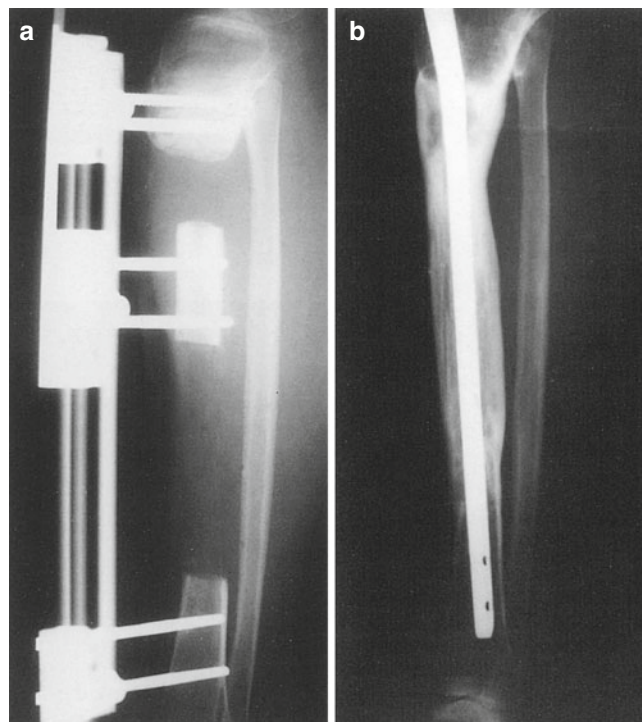
local pressure sores from an external prosthesis, phantom pain, and overgrowth of the stump when amputation is performed in children are recognized complications.

Endoprostheses are now used in a variety of benign and malignant conditions. There is a greater tendency to use them in malignant conditions, often where the patient's survival may be in doubt and hence the patient's longevity limited. Complex reconstructions are rarely justified in this situation. Although techniques such as osteoarticular allografting and bone transportation may be considered in patients with benign or low-grade malignant disease, there are occasions when endoprostheses may be utilized. In our practice, this is usually in periarticular destructive lesions, the most common of which being recurrent giant cell tumor. The frequency of prosthetic utilization in various pathologies is outlined in Fig. 23.24. It can be seen that less than 20 % of patients have a benign condition.

It is well known that most of the malignant bone and joint tumors have a predilection for the lower limb with a few cases occurring in the upper humeral metaphysis. It is therefore not surprising that if the distribution of prosthetic insertion throughout the body is studied, over 80 % of the cases have insertion in the lower limb. The proximal humerus remains the most common site replaced in the upper limb (Fig. 23.25). The foremost commonly replaced areas are therefore, in order of frequency, the distal femur and knee, the proximal femur and
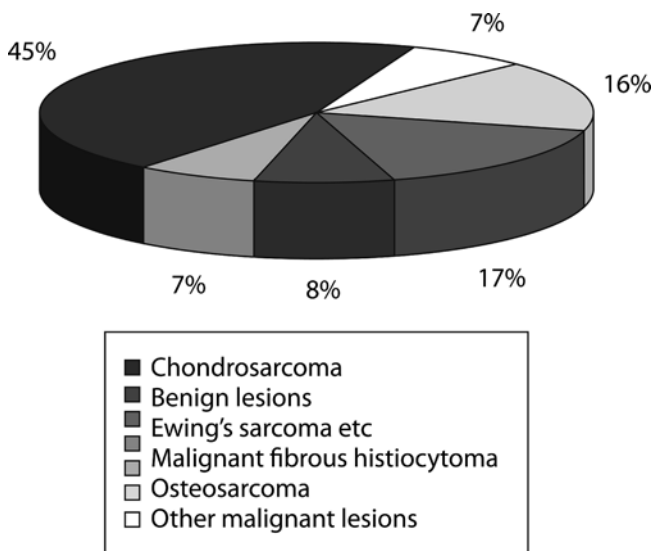
Fig. 23.24 Distribution of prosthetic utilization in various primary bone pathologies
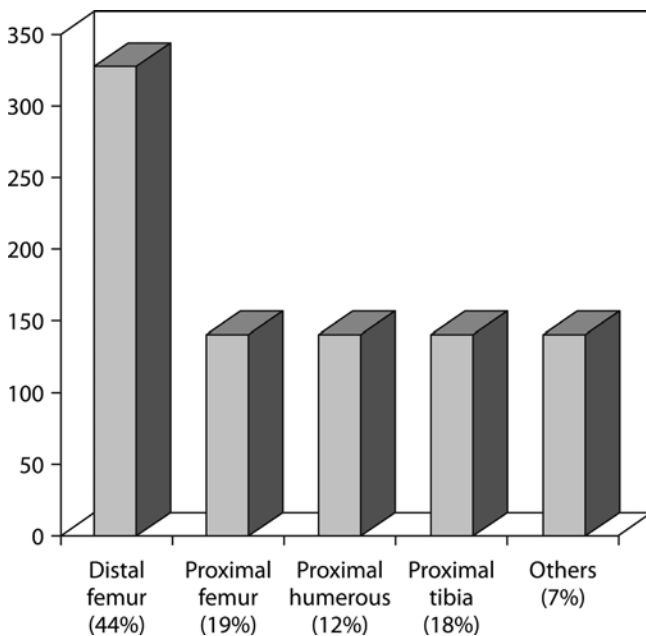


Fig. 23.25 Anatomical distribution of types of prostheses inserted

hip, the proximal tibia and knee and, last, the proximal humerus and shoulder. Occasionally, the diaphysis of femur, tibia, and humerus may be replaced, but these represent only a small fraction of the prostheses inserted. A similar low percentage exists for replacement of the whole bone and adjacent joints.

## Allograft Techniques

Allografts suitable for osteoarticular reconstruction are usually only retrieved from deceased donors. This leads to a sig-

nificant risk of human immunodeficiency virus (HIV) infection and secondary testing of the do nor cannot be accomplished [121]. Such allografts are rarely used in a fresh situation and they must either be frozen with cartilage cryopreservation or freeze dried. Similarly, they must be sterilized by either ethylene oxide or gamma irradiation. Only frozen techniques will allow attempts at cartilage cryopreservation, but frozen and freeze-dried techniques tend to reduce the antigenicity of the allograft. When implanted, the bio logical response to a preserved allograft is, at first, similar to an autograft. However, secondarily, there is an immunological response which causes changes within the graft. The immunological response mounted by the host causes vascular necrosis, which is followed by a second peak of osteoblastic activity at the end of the first 4 weeks. There has been some experimental work by Musculo [122] that suggests tissue typing in allografts will lead to better incorporation. Union of the allograft usually occurs from creeping substitution from the host bone, but there is usually excellent attachment of the soft tissues with the graft. The long-lasting presence of necrotic and revascularizing bone makes allografts more likely to fracture, but this is more of a problem in the lower limb. Strengthening of the allograft may be obtained by adding mechanical support or intramedullary cement. The overall fracture incidence is approximately 16 % [123]. The overall complication rate and long-term function of proximal humeral allografts has been reported by O'Connor et al. [124] and in a nonrandomized comparison of long-term function osteoarticular allograft functioned better than prostheses in the upper humeral position. This essentially has been due to better soft tissue re construction, and conforms with the previous work of Gebhardt et al. [125]. Many of the complications of allograft use in the long term have resulted from the lack of vascularity. Capanna et al. [126], have recently described a technique of using allograft shells combined with a vascularized fibular graft. This has not yet been used in an osteoarticular allograft, but may be of use where a scapulohumeral fusion is employed as the reconstructive method. While Mankin from the USA has popularized the use of cadaveric allografts, and although function in the upper limb is better than in the lower, there remain problems of sizing, stability, fracture, rejection, and degeneration [127, 128].

## Endoprosthetic Techniques

Each area which is replaced has its own particular problems, and these are illustrated below.

### Case 1
A 12 year old boy presented with a 5 week history of pain and discomfort in the left shoulder which was ignored. While on

holiday he fell from a donkey and sustained a pathological fracture. Staging investigations confirmed a pathological fracture through the left proximal humerus with no evidence of metastatic disease (Fig. 23.26). Biopsy confirmed high-grade osteosarcoma and the patient underwent neoadjuvant chemotherapy. The patient responded to chemotherapy and 6 weeks following the diagnosis underwent resection of the upper left humerus and endoprosthetic replacement (Fig. 23.27). The technical problems in performing upper humeral replacement in such a large tumor are twofold. The first is the proximity of the neurovascular bundle, part of which (the circumflex nerve) is particularly vulnerable as it winds round the surgical neck of the humerus. The second problem is the potential of intracapsular involvement of the glenohumeral joint. Fortunately, extra-articular resection is rarely required and in this case intra-articular resection was performed. There remains considerable debate as to the method of reconstruction of the residual rotator cuff. Early attempts to preserve function by sewing the cuff to a terylene sleeve were met with considerable abrasion debris and sinus formation. Some surgeons still use such a cuff as an artificial capsule over which the rotator cuff is repaired. This technique may lead to considerable stiffness of the glenohumeral joint. Prosthetic replacement of the upper humerus leads to excellent restoration of elbow and hand movement. Shoulder movement, however, remains quite limited. The usual outcome is that rotation is well controlled, although external rotation may be grossly exaggerated. Flexion and abduction are rarely better than 40°, and if the circumflex nerve is sacrificed may not be achieved at all. In manual workers where nerve sacrifice is anticipated, some form of biological or prosthetic arthrodesis of the glenohumeral joint may be a better alternative. Even where the circumflex nerve is preserved, rotator cuff function remains poor, and over time many prostheses sublux into the subacromial space. Early experience with bipolar prostheses where a reverse shoulder mechanism is utilized has shown much better functional movements without the risks of superior or inferior subluxation. The mechanism involves a hemisphere on a spiral component which is screwed into the glenoid with an HA collar. This snap fits into a concave surface inserted on to the upper humerus. Early 5 year results are now available and are encouraging [129].

## Case 2

A 12 year old boy presented with a 3 month history of pain and discomfort in the upper left femur. Initial investigation at another hospital showed an abnormal area on plain radiograph and this site underwent open biopsy, which showed Ewing's sarcoma. He was treated with chemotherapy and



**Fig. 23.26** Pathological Fracture through osteosarcoma of the proximal humerus
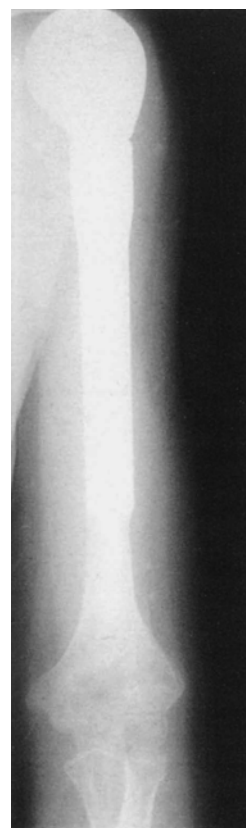


**Fig. 23.27** Proximal Humeral prosthetic replacement

**Fig. 23.28** Growing proximal femoral prosthesis with bi-polar head



**Fig. 23.29** Pathological fracture through osteosarcoma of the right distal femur

then underwent an intra-articular resection of the hip joint and upper third of the left femur. The prosthesis was inserted and a bipolar head placed on top of the prosthesis to give acetabular stability. The prosthesis was of an extendible variety (Fig. 23.28). The surgical technique involved detachment of the iliac psoas and all three gluteal muscles. It is usually possible to leave the tensor fascialata intact which preserves innervation. The rest of the vastus muscles remained innervated although the vastus lateralis may be denervated and vastus intermedius is usually excised as a barrier to the tumor. Two methods of reconstruction of the abductor apparatus are possible. Usually the soft tis sue is reconstructed using a nylon weave to connect the muscular structures to the tensor fascia lata. Abduction can be maintained but the altered lever arm means that many patients have a positive Trendelenburg gait. Another technique under investigation involves turning down part of the ilium attached to the anterior fibers of gluteus medius muscle to allow fibrosis of the muscle on to the prosthesis itself. The most frequent complication of this procedure is hip dislocation. The patient is
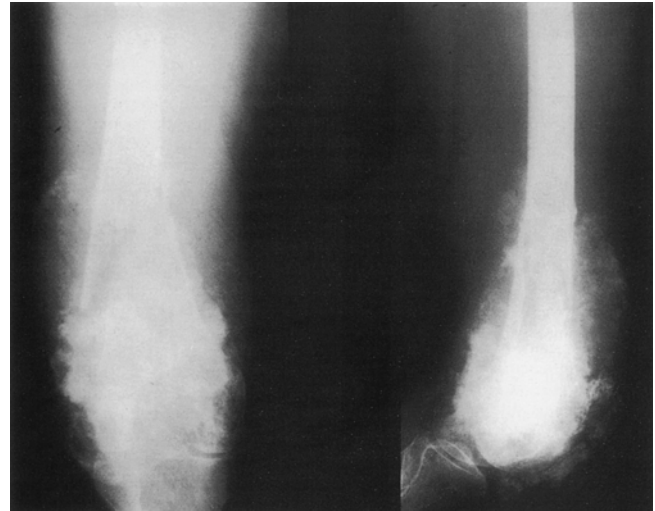
advised to use a PoHo type brace for the first 2 months after operation

### Case 3

An 8 year old girl presented with a 2 week history of pain in her right distal femur and awoke one morning following a tussle with her sibling in excruciating pain. Plain radiograph confirmed an undisplaced pathological fracture through an osteosarcoma of the distal right femur (Fig. 23.29). Percutaneous needle biopsy performed under general anesthesia confirmed a chondroblastic osteosarcoma. The patient received neoadjuvant chemotherapy and underwent resection of the tumor 6 weeks later. Analysis of the resected specimen confirmed 90 % of the tumor had under gone complete necrosis. It was opted to reconstruct the limb using an uncemented expandable prosthesis (Fig. 23.30). The patient had an uneventful postoperative recovery and is now walking without a limp. Distal femoral replacement remains the most successful area in terms of early function following prosthetic insertion. The anatomy of the region means that the extensor apparatus is rarely severely damaged, and although the gastrocnemius is severely weakened by detachment of their origins, knee flexion can be fully compensated by the hamstrings. Therefore, it is often difficult to tell the operated side when observing gait in such patients. The mechanism used in this case to enable elongation of a prosthesis is termed minimally invasive. Elongation is achieved by insertion of an Allen key to turn a low gear mechanism to achieve elongation of the body of the prosthesis. It is, however, likely that this young lady will require a revision of her prosthesis and perhaps surgical cessation of growth on the opposite limb in order to achieve limb balance at maturity. Over the last 2 years, increasing use of noninvasive magnetic endo-

**Fig. 23.30** Uncemented extendible distal femoral and knee prosthesis



**Fig. 23.31** X-ray of osteosarcoma of proximal tibia showing large tumour with soft tissue extension

prosthesis has been experienced. The prosthesis is similar to the prosthesis described above, but here the elongation is achieved by a motor placed within the body of the prosthesis. Placing the motor in a magnetic field produces a force of around 1500 N, which allows very slow extension of the prosthesis. Some 4 mm of extension will be achieved in 16 min. The slow but strong elongation force is achieved by using an epicyclic gear box. To date the prosthesis is used mainly in the lower limb prosthesis where growth is more important, but experience is just beginning regarding the humerus [130].

**Case 4**

A 17 year old boy presented with a rapidly enlarging swelling of the left proximal tibia. He denied any pain. Plain radiographs revealed a lytic area of the upper tibia through an area of abnormal bone. Jamshidi needle biopsy performed under local anesthetic confirmed an osteoblastic high-grade osteosarcoma; x-ray showed a typical osteosarcoma with significant soft tissue mass (Fig. 23.31). Further staging investi-

gations revealed no evidence of metastatic disease. The patient received neoadjuvant chemo therapy, which was uncomplicated, and 6 weeks later underwent prosthetic replacement of the right proximal tibia. The surgical resection of the proximal tibia is fraught with complications. The most important of these as regards long-term function is the detachment of the extensor mechanism. The next most common problem concerns the common peroneal nerve, which usually has to be mobilized and occasionally sacrificed in resection of the tumor. The vascular structures are closely applied to the posterior aspect of the knee and the anterior tibial artery is nearly always sacrificed, as it is grossly adherent to the tumor as it enters the anterior compartment. The early morbidity in these cases, therefore, usually is a combination of arterial ischemia, compartmental syndromes, and nerve palsy. Established neural palsy is, of course, treatable by use of an
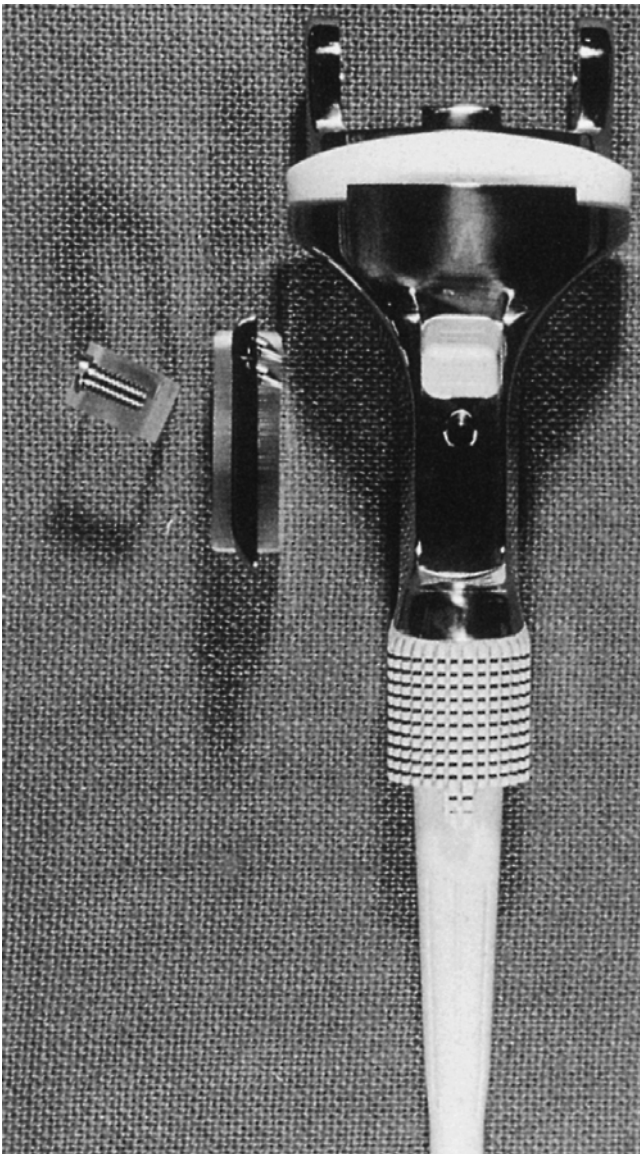
**Fig. 23.32** Proximal tibial prosthetic replacement

external ankle-foot orthosis (AFO), ankle arthrodesis or, where appropriate, tendon transfer. In the long term, the major functional disability lies in the weakness of the extensor mechanism. All upper tibial replacements undergo a medial gastrocnemius flap, and this further weakens the flexors of the knee, the long flexors having been previously detached. The extensor mechanism may be reconstructed by simple suture on to the transposed medial head of gastrocnemius, but others prefer a transposition of the upper fibula achieved by multiple osteotomy if this bone is still present or by turndown of a portion of the distal patella (Fig. 23.32).

Postoperative rehabilitation is slow, and the patient is usually kept splinted in extension for a period of 6–8 weeks. The area of reconstruction of the extensor mechanism usually stretches, and the patient usually presents with patella alta

and occasionally instability. Few can achieve a straight leg raise, although most achieve a normal walking pattern. This is achieved by throwing the tibia forward following hamstring relaxation and then locking the prosthesis in slight hyper extension.

## Amputation and Disarticulation

Despite the current trend to perform limb salvage procedures in malignant disease following neoadjuvant chemotherapy, there are still a proportion of patients who are not suitable for this technique. The present primary amputation rate for musculoskeletal bone tumors at the Royal National Orthopaedic Hospital is 7 %. The indications for primary amputation are as follows:

1. Late presenting tumors with widespread soft tissue contamination, including involvement of the neurovascular bundle, which do not respond to chemotherapy;
2. Difficult anatomical location where tumors surround the neurovascular bundle ab initio;
3. Advancement of tumors despite chemotherapy (poor response to chemotherapy);
4. Wide major displacement and pathological fracture at presentation.

The description of various techniques of amputation is not in the remit of this chapter. However, the most usual lesion which requires amputation is the proximal humeral osteosarcoma where there is widespread involvement of the axillary structures, often with encroachment onto the chest wall. Simple disarticulation of the glenohumeral joint is rarely sufficient in gaining tumor control. These patients unfortunately, require a forequarter amputation procedure.

## Management of Local Recurrence

When the first meeting of the International Limb Salvage Association occurred at the Mayo Clinic in 1981, the goal of the symposium was to share experience and focus research into improved results of limb-sparing procedures. At that meeting, the local recurrence rate for all the reported series of limb salvage procedures was 4 %. The society has continued to meet on a twice-yearly basis, and techniques of limb salvage have been popularized. The difficulty is that despite improved imaging techniques, the local recurrence rate for malignant tumors is now 10 % (Enneking WF, personal communication). This seemingly detrimental step in terms of treatment of course results from a vast increase in the number of procedures performed and also a change in patient awareness and demands. Local recurrence usually occurs within 2

years from the primary procedure and the surgeon must be ever aware of its possibility. All limb salvage procedures have in common a very narrow resection margin at the level of the neurovascular bundle. It is not surprising that the majority of local recurrences tend to occur adjacent to this structure. To date, in the series at the Royal National Orthopaedic Hospital, London, we have had only one true recurrence within bone; 50 % of local recurrences, because of involvement of neurovascular bundles, require either disarticulation or an ablative procedure in order to clear the problem. It is important that before undergoing such a procedure the patient is restaged for the presence of metastatic disease. Where local recurrence occurs in tumors not adjacent to neurovascular structures but adjacent to bone, further resection and radiotherapy may be feasible.

## Rehabilitation

The majority of limb salvage surgery procedures for primary bone tumors tends to occur in specialized units. Within those units are skilled physiotherapists and occupational therapists who have a wide experience in the rehabilitation of such difficult patients. The aim of biological reconstruction is not to use prolonged immobilization of joints and, therefore, removable splints rather than plaster fixation is generally preferred. Wherever possible, sound primary internal fixation of bone grafts is utilized. There is a continuing debate as to the effect of radiotherapy and chemotherapy upon biological fixation, and this appears to be greater if intra-arterial chemotherapy is considered [131]. Certainly in present regimes patients must be returned for further chemotherapy as rapidly as possible, and where a positive tumor margin is found in the tumor resection, radiotherapy must be considered in addition to attain local control. At present, radiotherapy can be administered in an interval between chemotherapy courses, and occasionally in a hyper-fractionated manner. This is an extremely time consuming and difficult technique, and more traditional approaches have been to delay radiotherapy until primary chemotherapy has been completed. Where patients have received an endoprosthesis, there is no concern regarding union of allograft to host or incorporation of graft, and therefore postoperative oncological management can begin as soon as the wound condition is satisfactory. With endoprosthesis of the proximal humerus, the lack of reliable reattachment of the rotator cuff or denervation or excision of the deltoid leads to significant problems with functional abduction and flexion of the shoulder joint. Although rapid mobilization of the el bow and distal limb is achieved, functional control of the shoulder is only slowly achieved, often not till approximately 6 months. At best, without a rotator cuff, only 40° of flexion and abduction are achieved, although good rotational control of the limb is usually achieved by 6 months.

Some early work is being per formed on motorized abductor function by rotatory grafts of innervated latissimus dorsi. Whether this will achieve improved function in the long-term is still unclear. Careful evaluation of the patient is required in the pre-surgical period as arthrodesis of the shoulder is probably more suitable for a manual worker.

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