11

Treatment of Metastatic Bone Disease

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OVERVIEW

Few skeletal metastases require surgical intervention. Radiotherapy, chemotherapy or both often provide symptomatic relief. An impending or actual pathologic fracture requires operative fixation because fractures through a tumor-bearing bone rarely heal without such intervention.

The goals of fixation are to relieve pain, improve function and ambulation, facilitate medical and nursing care, and improve psychological well-being (Figures 11.1 and 11.2). The primary functional goal of surgical intervention is to allow immediate weight-bearing. Surgery should be avoided if this cannot be achieved. A variety of techniques, including prosthetic reconstruction (especially about the hip) or a combination of internal fixation combined with polymethyl methacrylate (PMMA), provides immediate fixation and stability. After the wound has healed, radiotherapy is usually used to arrest local tumor growth, permit bony repair, and prevent re-growth of tumor around the fixation device. This chapter discusses the techniques of treatment of long bone metastases.

INTRODUCTION

The role of the orthopedic surgeon in the management of skeletal metastases is to: (1) confirm the diagnosis; (2) treat pathologic fractures; and (3) monitor patients at risk for pathologic fracture. Surgery can play an important role in reducing pain, improving function, and increasing quality of life, even in patients with very short life expectancies. Additionally, aggressive treatment of solitary skeletal metastases may improve long-term survival in selected patients. For example, patients with renal cell cancer and a solitary skeletal metastasis amenable to wide resection can achieve a 30–35% 5-year survival.

All cancer patients with new onset of pain must be assumed to have a skeletal metastasis until proven otherwise. The initial evaluation of such a patient, however, must not rule out the possibility that the lesion is unrelated to the cancer. In approximately 45% of cases a solitary hot spot seen on a bone scan in a cancer patient otherwise free of disease is associated with an unrelated process. Needle biopsy has been shown to be effective in diagnosing skeletal metastases in patients with a history of cancer. Most patients, however, present with multiple skeletal lesions, making the diagnosis of metastatic disease certain.

With few exceptions, patients who present with a painful pathologic fracture are candidates for surgical intervention. Management must be tailored to the individual; this entails balancing the benefit of surgery

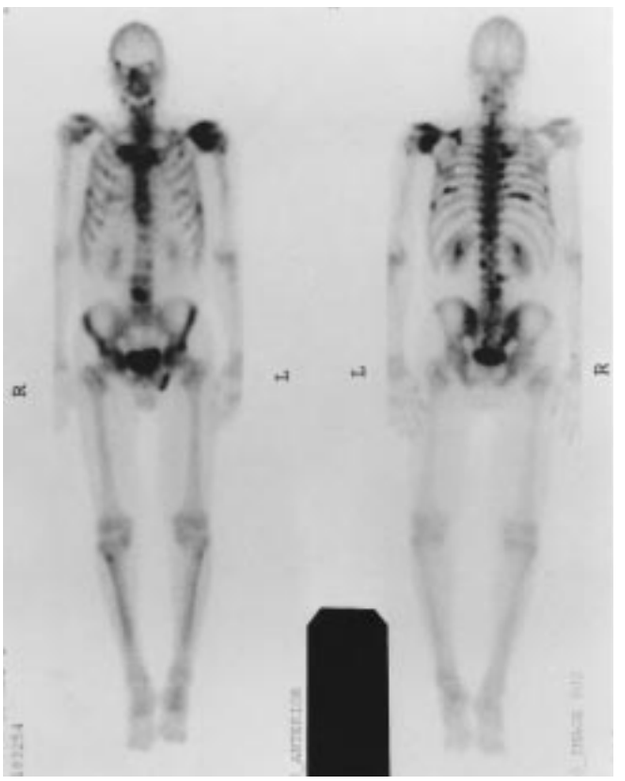

Figure 11.1 Three-phase bone scan showing multiple "hot spots" involving the ribs and shoulder girdle. This demonstrates the typical spread of carcinoma to the skeletal system.

Figure 11.2 Composite photograph showing several types of proximal femoral replacements used to reconstruct large skeletal defects following the resection of metastatic tumors of the proximal femur. The prosthesis (arrow), is a custom prosthesis to replace approximately one-half of the femur. The other two prostheses are modular prostheses that are also utilized in the treatment of primary bony sarcomas. The major indications for segmental replacement of the proximal femur are large, destructive, lytic lesions involving the head, neck, and shaft; solitary metastases; and recurrent tumor following previous attempts at intramedullary fixation with or without cementation.

and the risks associated with operating on a patient with a limited life expectancy and who is in poor medical condition. Isolated fractures of non-weight-bearing bones in the upper extremities can frequently be managed with palliative radiotherapy and casting or bracing. A patient with lower-extremity lesions requires greater use of the upper extremities for transfers and crutch or walker-assisted ambulation. Under these circumstances surgical intervention is often essential. All extremities must be carefully examined before embarking on a course of treatment.

The goals of surgical fixation are to relieve pain, improve function and ambulation, facilitate medical and nursing care, and improve psychological well-being. This requires a different approach from that used for non-neoplastic lesions. Immediate fixation must be obtained at the time of surgery: these patients rarely tolerate multiple surgical procedures. Bony union almost never occurs without surgery and radiotherapeutic treatment. The basic principle of surgical management is internal fixation or prosthetic replacement combined with PMMA. Cementation permits immediate stability and early mobilization and pain reduction.

IMPENDING PATHOLOGIC FRACTURES

Any skeletal lesion may cause a pathologic fracture. Criteria for selecting patients for prophylactic fixation have slowly evolved. Early criteria were based solely on retrospective observations of pathologic fractures in the proximal femur and hip. This was of great importance to orthopedists because of the technological difficulty in fixing such fractures, as well as the high mortality rates associated with hip fractures (Figures 11.3 and 11.4).

The first set of combined guidelines (1986) for prophylactic fixation of proximal femur were:[1] (1) greater than 50% cortical destruction seen on CT, (2) a lytic lesion of the proximal femur > 2.5 cm in diameter, and (3) avulsion of the lesser trochanter. While these guidelines were helpful for lytic lesions of the femur, they failed to account for other patterns of mixed or permeative lesions and would not be readily applied to other sites. In addition, these guidelines failed to account for lesions amenable to nonsurgical treatments. Increasingly, effective adjuvant treatments have resulted in improved patient survival, increasing the time at risk for any given lesion to fracture. Therefore,

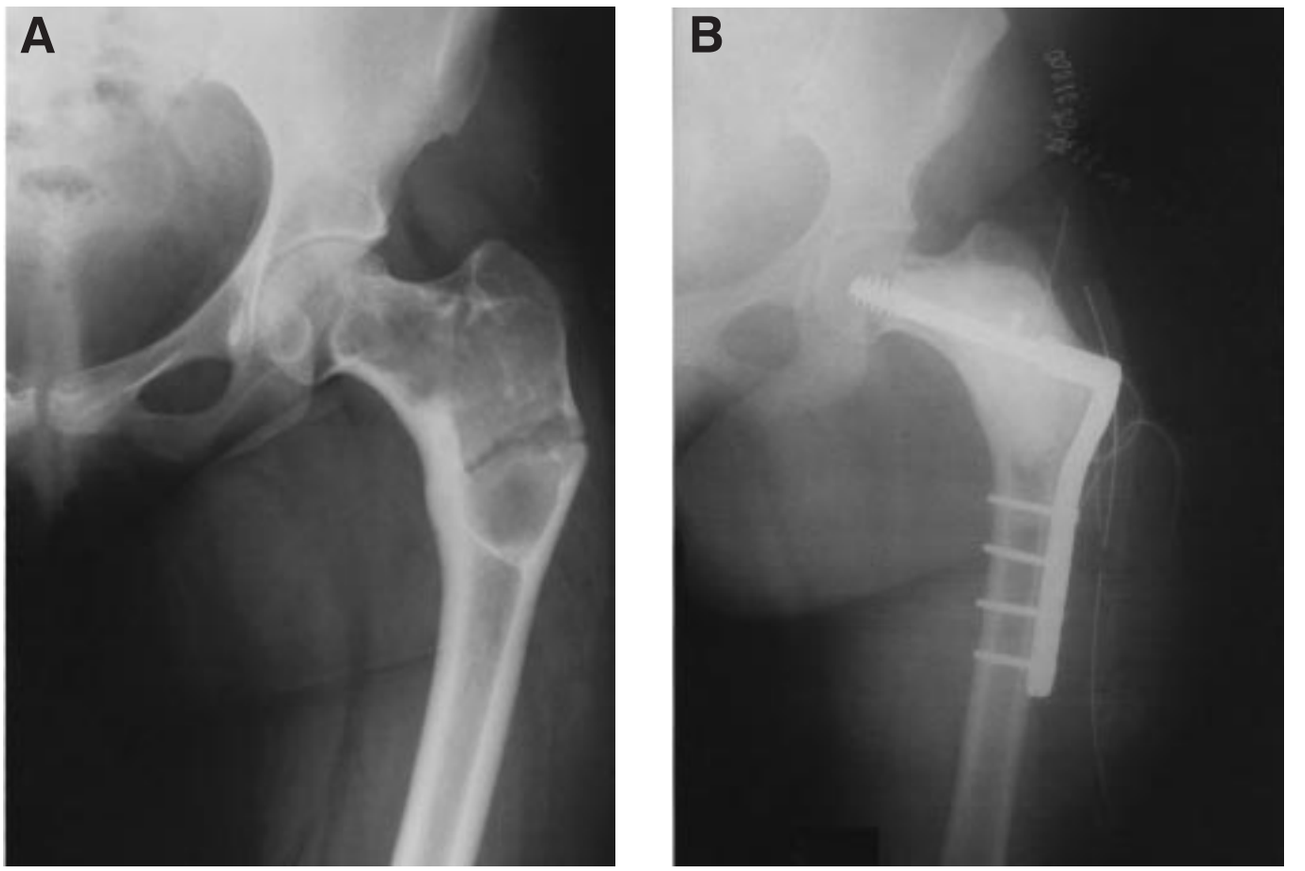

Figure 11.3 *(see above and following page).*

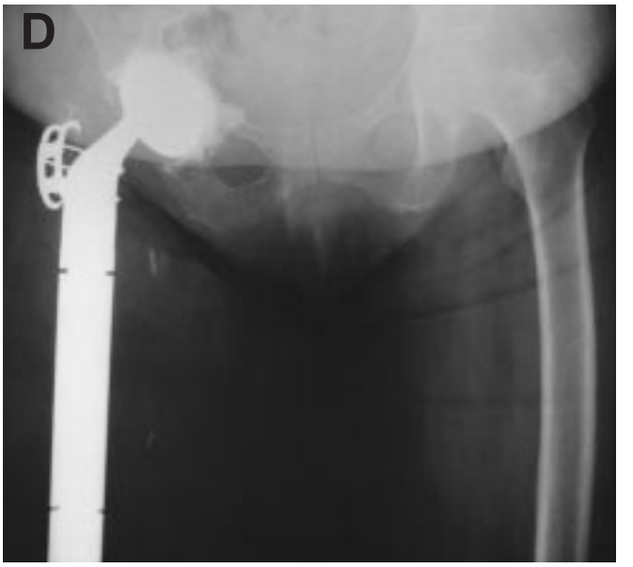

Figure 11.3 (**A**) Plain radiographs of the fixation of a multiple myeloma of the lesser trochanteric region of the proximal femur which has progressed despite radiation therapy and fractured with a plate and screws in place. (**B**) Postoperative radiograph following resection of the proximal femur.

Thompson[2] revised the Harrington[1] criteria defined as follows: (1) large lytic lesions occupying 50% or more of the cortical diameter unless protected until reconstituted with radiation therapy, medical management, or both; and (2) all destructive lesions of the femoral neck in patients with a survival estimate of > 3 months.

PREOPERATIVE EVALUATION AND INTERVENTIONS

Special preoperative considerations are needed because these patients often have extensive metabolic, hematologic, and nutritional deficiencies. The risk of infection is increased because of possible multiple sources of sepsis (e.g. colostomy, urinary tract infection), neutropenia from chemotherapy or other adjuvant modalities, generalized nutritional deficits, and poor local skin condition from prior radiotherapy or other procedures. Perioperative antibiotics are recommended for all patients. All patients should have hematologic and clotting evaluation, because many may suffer from anemia of chronic disease or depletion of clotting factors because of a vitamin K deficiency or tumor involvement of the liver. Adequate blood replacement should be available because curettage of many carcinomas – especially myeloma, thyroid tumor, and renal cell carcinoma – often leads to substantial blood loss. The combination of pre-existing anemia and expected blood loss mandates the use of preoperative blood transfusions. Thrombocytopenia occasionally occurs intraoperatively and should be treated aggressively when it occurs. Disseminated intravascular coagulation (DIC) has been noted.

As many of these patients are older, coexisting diseases (e.g. hypertension, diabetes, renal insufficiency, peripheral vascular disease, and cardiopulmonary disease) must be identified and controlled. The presence of other sites of skeletal disease may require special precautions at the time of surgery to prevent additional pathologic fractures. Rib involvement, common in advanced multiple myeloma, may make respiration difficult, leading to prolonged or permanent ventilator dependence following general anesthesia. Specific disorders associated with skeletal metastases

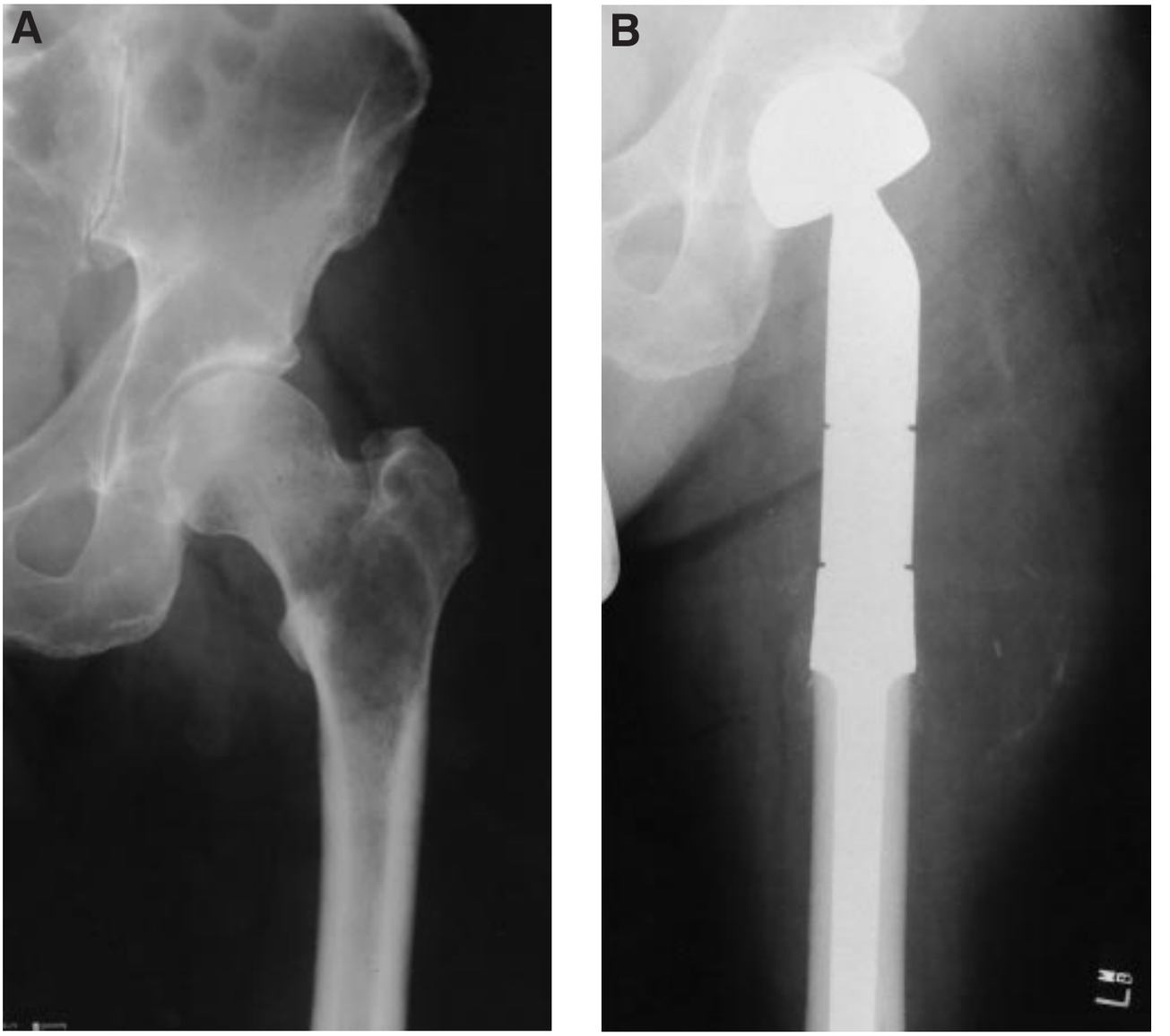

Figure 11.4 Plain radiographs showing a large lytic lesion of the proximal femur secondary to a solitary renal cell carcinoma (**A**). This patient was treated by a proximal femoral modular segmental replacement (**B**). It is the choice of the authors to utilize segmental replacements for solitary metastatic tumors, especially renal cell carcinomas, melanomas, and thyroid carcinomas.

must also be controlled. Of particular concern is hypercalcemia, which can lead to sudden death during anesthesia. The use of bisphosphonates, including pamidronate, have been shown to be effective in reducing the serum calcium to normal levels.

Evaluation of the extent of local disease, the amount of bone involved, and the presence of multiple lesions within the same bone are necessary to determine the optimal surgical approach, the amount of tumor to be removed, and the method of reconstruction. The following are studies commonly used; the choice of imaging techniques depends on the individual patient and tumor location and type.

Bone Scintigraphy

Technicium-99 bone scans can demonstrate the intraosseous extent of tumor and the site of the lesion: whole-body scanning provides information about other possible sites of disease. Additional lesions are

commonly found within the same bone. All lesions within the same bone generally require simultaneous treatment; this usually requires placement of an IM rod or an extended-length endoprosthesis.

Computed Tomography and Magnetic Resonance Imaging

Computed tomography remains the standard for evaluation of cortical bone involvement and is required for lesions of the pelvis, shoulder girdle, and spine. With the exception of lesions being evaluated for prophylactic fixation, it is rarely required for extremity lesions. Tumors of the bony pelvis often have large soft-tissue components that may bleed excessively or lead to mechanical failure of the reconstruction if not recognized preoperatively. MRI is most useful in the evaluation of the soft-tissue extent of the tumor. It can also reveal intramedullary tumor involvement.

Angiography

Diagnostic angiography is not routinely performed; specific indications are pelvic tumors with large extraosseous components and lesions in which preoperative embolization is considered. Patients with metastatic hypernephroma are routinely treated with preoperative embolization because of the potential for extreme, uncontrollable bleeding at the time of surgery (Figure 11.5).

PRINCIPLES OF SURGICAL TREATMENT FOR SKELETAL METASTASIS

Advances in orthopedic techniques and implants have dramatically increased the treatment options for patients with skeletal metastases. Improved metallic alloys, introduction of third-generation interlocked IM rods, advanced prosthetic design, modular segmental replacement endoprostheses, rigid segmental spinal systems, and vertebral body cages permit reconstruction of even the most challenging pathologic fractures. PMMA, used as an adjunct to fixation devices (intramedullary rods,

Figure 11.5 *(see above and following pages).*

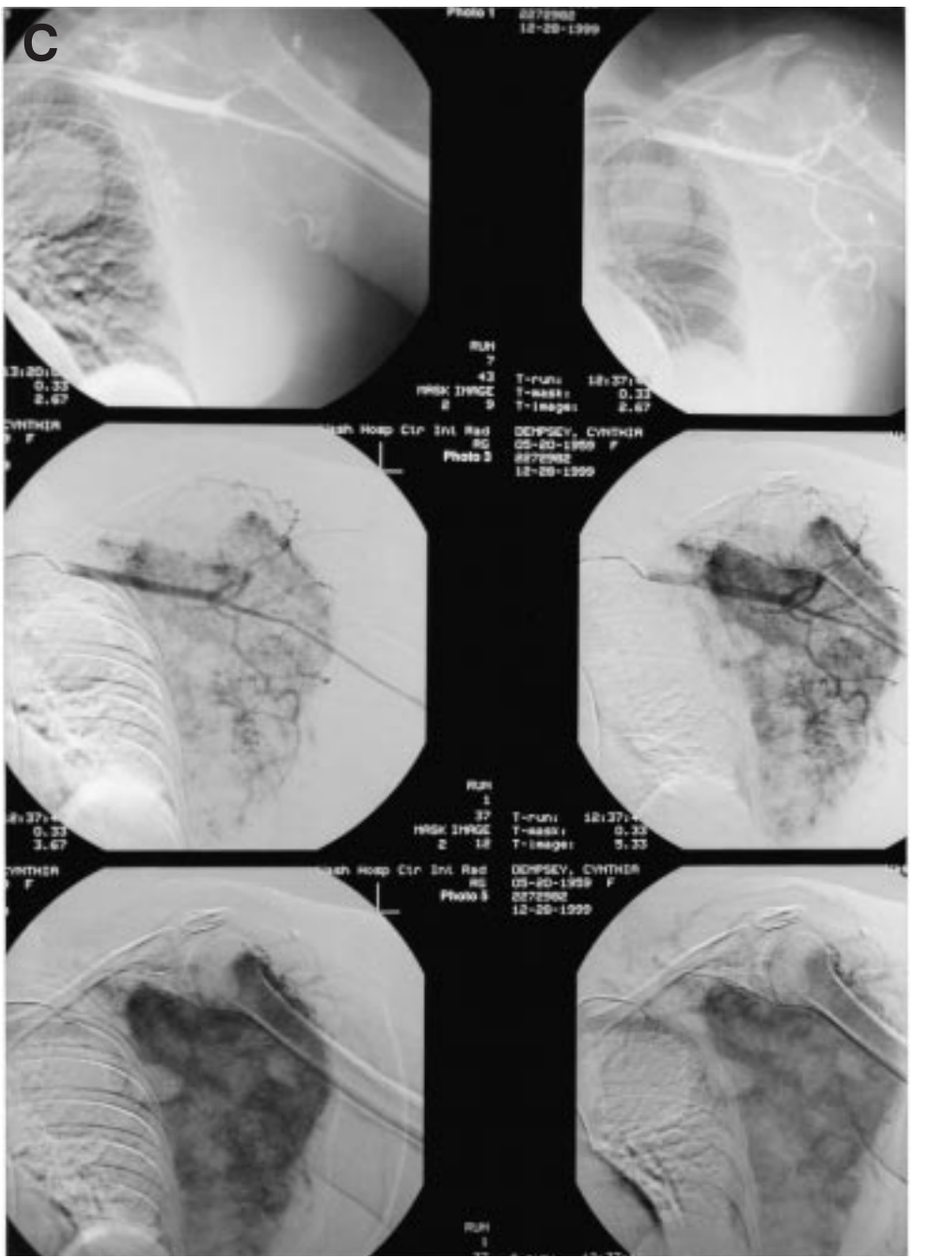

Figure 11.5 *(see above and following page).*

plates and screws) and prostheses permits instant filling reconstruction of large defects and immediate stabilization. Adjuvant treatment of the tumor is necessary to protect the reconstruction. Therefore, all patients with skeletal metastases require a multidisciplinary approach coordinating chemotherapy and radiation with surgical intervention.

Principles of management of pathologic or impending fractures are as follows:

1. Preoperative embolization of suspected vascular tumors.
2. Administration of perioperative antibiotics.
3. Correction of underlying hypercalcemia.
4. Transfusion to correct pre-existing anemia, thrombocytopenia and coagulation deficits.
5. Modification of standard surgical approaches to avoid prior radiation fields and ensure adequate soft-tissue coverage and closure.

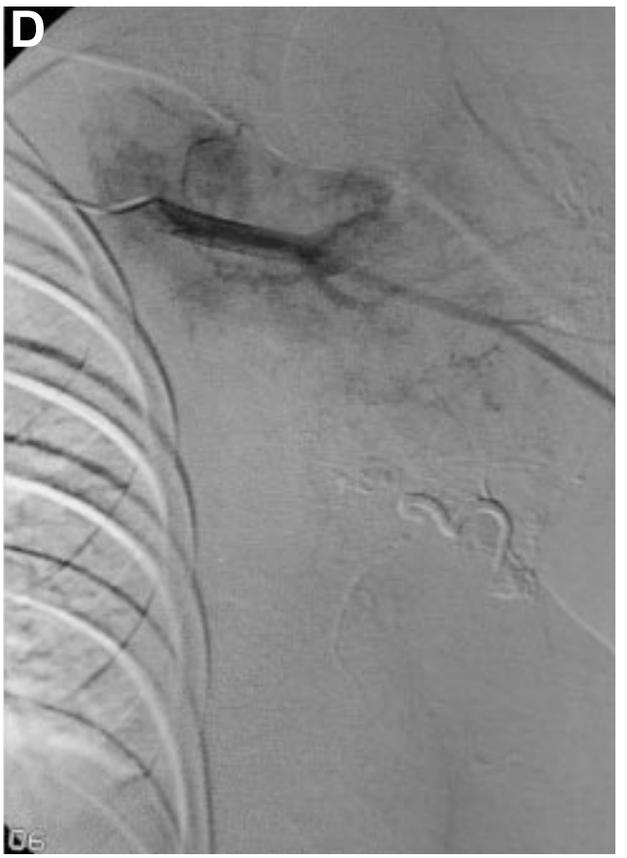

Figure 11.5 Angiography with embolization of a large metastatic thyroid carcinoma to the right periacetabulum. The superacetabular region is a common area for metastatic disease from renal cell and thyroid carcinomas. (**A**) Plain radiograph prior to embolization. (**B**) Angiography following embolization showing absence of vascular blush within the superacetabular region. Note: this patient had undergone a prosthetic replacement of the hip for a stress fracture through irradiated bone unrelated to the carcinoma. The curved arrow indicates the obliteration of the hypogastric (internal iliac) artery which has been embolized prior to surgery. Solid arrows show the periacetabular area with complete absence of tumor vascularity. (**C**) Angiography of a large renal cell carcinoma replacing the entire scapula; time sequence injection study. (**D**) Post-embolization showing almost a complete absence of vascularity. This patient was treated by a total proximal humerus and scapula resection (Type IV).

6. Curettage to remove all gross disease.
7. Use of immediate rigid fixation consisting of internal fixation with PMMA or cemented prosthetic replacement.
8. Filling of defects with PMMA.
9. Postoperative nutritional supplementation to promote wound healing.
10. Adjuvant radiotherapy, with or without adjuvant chemotherapy.

The common local surgical procedures for metastatic tumors of the extremities are: tumor excision, composite osteosynthesis, joint replacement, segmental reconstruction, cryosurgery and amputation.

Tumor Excision

Tumor removal and bone stabilization best meet the goals of diagnosis, functional stability, and pain relief. For this reason the metastatic lesion should generally be curetted. Treatment options include intralesional (marginal) and extralesional (wide) excision. Intralesional curettage of tumor is usually performed in or around a fracture site at the time of stabilization (Figure 11.6). Extralesional excision, i.e. resection, is usually performed for a solitary metastatic lesion.

Composite Osteosynthesis

Internal fixation devices (bone plates, screws, IM rods and nails) are used to stabilize impending or actual pathologic fractures. This technique is most often used for metastatic lesions in the shaft diaphysis of long bones, most commonly the humerus and femur.

Joint Replacement

Joint replacement entails resection and reconstruction of a joint using a prosthesis combined with PMMA. Hemijoint replacement involves resection of half of the joint surface and adjacent bone. Total joint replacement is rarely required. Metastatic lesions of the proximal femur are most commonly treated by endoprosthetic replacement.

Segmental Reconstruction

Segmental reconstruction is the resection of a large segment of bone combined with segmental prosthetic replacement and PMMA. This technique is less common than joint replacement and is used for large lesions for which the remaining bone cannot be reconstructed by cementation and internal fixation (Figures 11.7 and 11.8).

Cryosurgery

Cryosurgery is the use of liquid nitrogen as a surgical adjunct to tumor curettage to freeze any residual tumor cells. It may be combined with any of the above procedures in order to increase local tumor control.

Figure 11.6 Anterior–posterior (**A**) and lateral (**B**) plain radiographs following curettage, cryosurgery, cementation, and internal fixation of a large lytic lesion of the proximal tibia for a metastatic melanoma. Cryosurgery was utilized in an attempt to gain local control in addition to postoperative radiation therapy.

Amputation

Amputation has a limited, but definite, role in the management of metastatic cancer. It is occasionally indicated only when advanced cancer results in uncontrollable or intractable pain, a functionless extremity, tumor fungation, sepsis, or erosion and hemorrhage of a major vessel at the tumor site. These complications occasionally occur after inadequate local tumor control. The goal of amputation is to eliminate pain or sepsis and restore function.

Forequarter amputation may be required for recurrent breast carcinoma involving the brachial plexus and axillary vessels.

SPECIFIC ANATOMIC SITES

Pelvis and Acetabulum

Lesions of the hemipelvis not directly involving the hip joint can generally be treated with modification of weight-bearing and external beam radiation. Avulsion

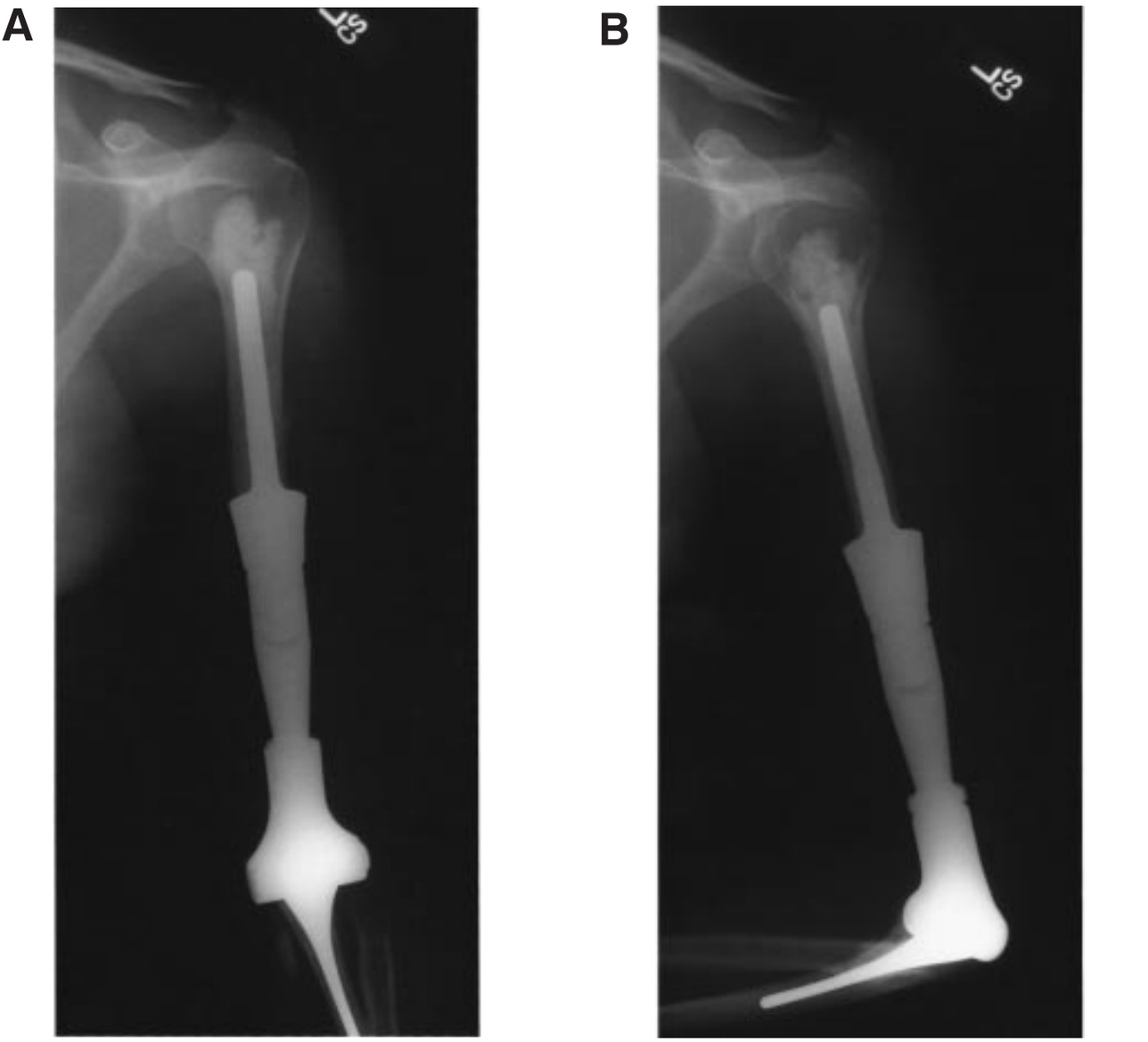

Figure 11.7 Anterior–posterior and lateral photographs of a large segmental replacement of the distal humerus and elbow joint for a large destructive melanoma of the elbow (**A**) shows the AP view; (**B**) shows the lateral view. Melanomas, similar to renal cell carcinomas, may cause large lytic destruction of a bone simulating a primary sarcoma. Local control is often difficult to obtain. The authors prefer resection of large metastatic melanomas in-lieu of curettage and cementation.

fractures of the anterior superior/inferior iliac spines, iliac crest, and superior/inferior pubic rami are common and should be treated nonoperatively. Large supra-acetabular lesions that do not respond to radiotherapy should be curetted and packed with PMMA combined with Steinmann pin fixation (Figures 11.9 and 11.10).

Proximal Femur (Hip)

The hip is most common site of pathologic fracture. This is because of the high incidence of metastases in this area and the magnitude of force concentrated in this area with normal activity. In general, all pathologic

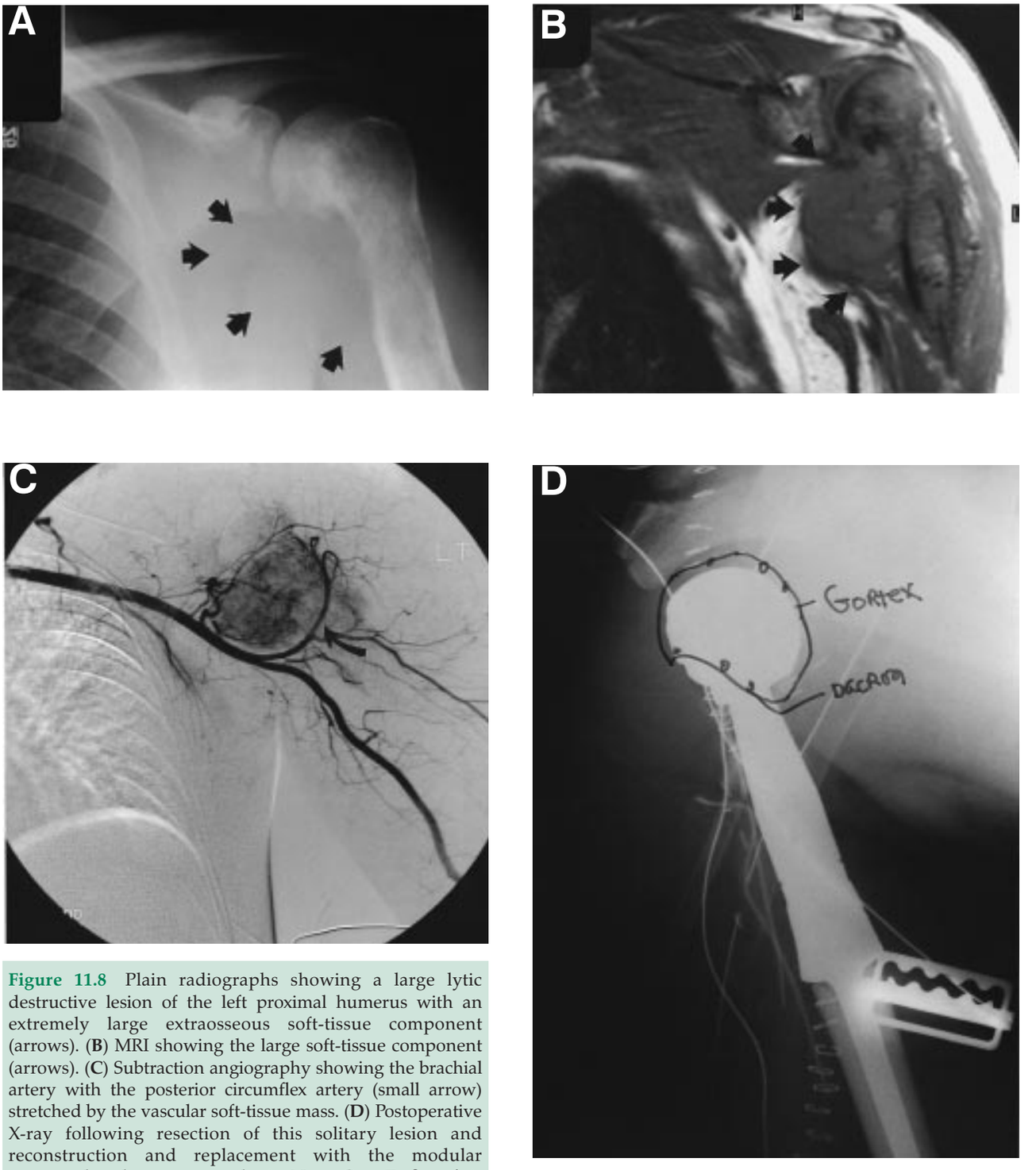

Figure 11.8 Plain radiographs showing a large lytic destructive lesion of the left proximal humerus with an extremely large extraosseous soft-tissue component (arrows). (**B**) MRI showing the large soft-tissue component (arrows). (**C**) Subtraction angiography showing the brachial artery with the posterior circumflex artery (small arrow) stretched by the vascular soft-tissue mass. (**D**) Postoperative X-ray following resection of this solitary lesion and reconstruction and replacement with the modular segmental replacement prosthesis. Note: Gore-Tex® graft is utilized to stabilize the humeral head, neck, and glenoid joint. The Gore-Tex® is reinforced by Dacron tape as noted. Large solitary metastatic tumors to the skeletal system with large extraosseous components are best treated by primary resection.

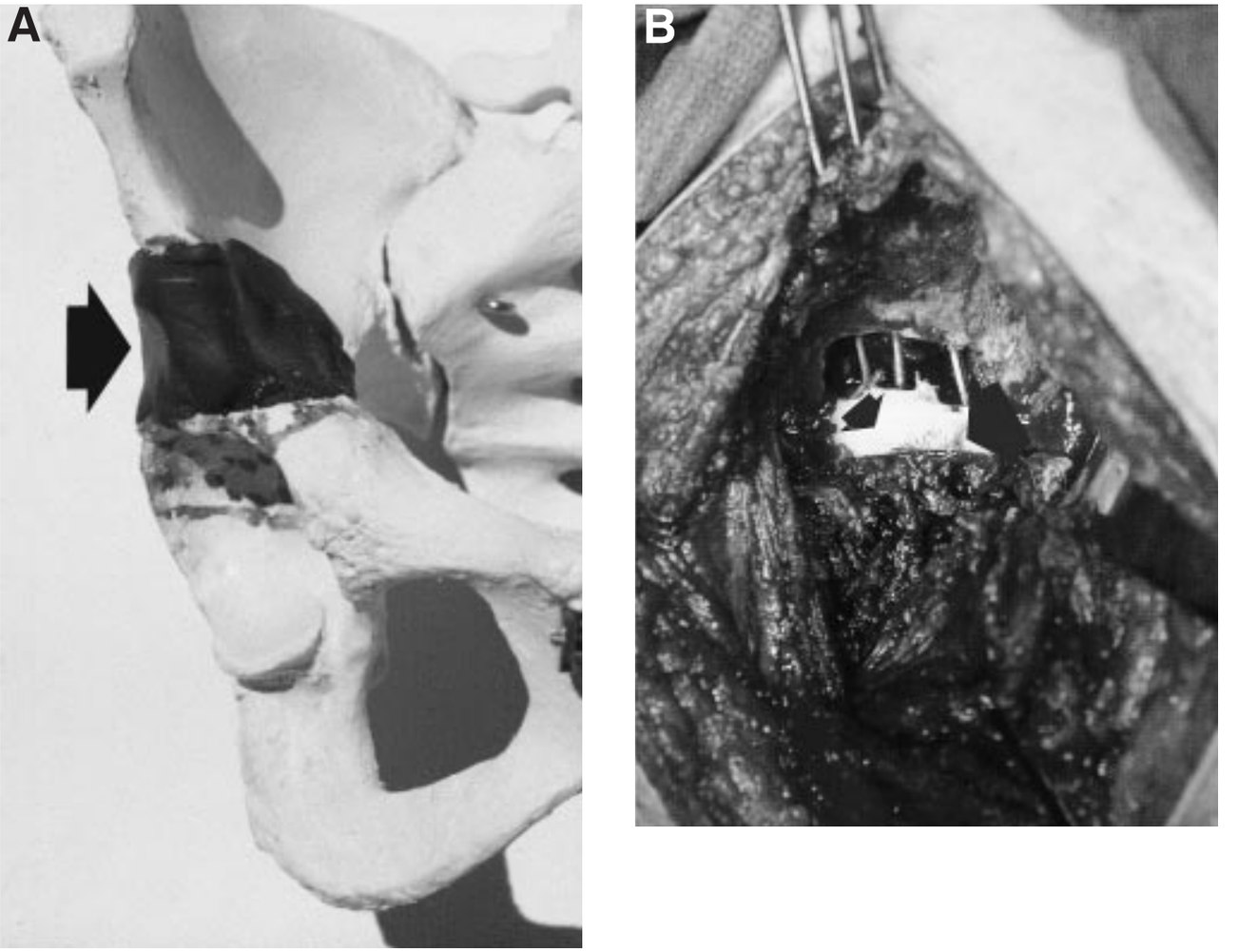

Figure 11.9 (**A**) A plastic model of the pelvis with a large superacetabular tumor demarcated by the dark area (arrow). The superacetabular area of the ilium is a common area of metastases for many types of carcinomas, especially metastatic renal cell carcinoma and thyroid carcinoma. (**B**) Intraoperative photograph showing a curetted defect corresponding to the lesions seen in (**A**) and reconstructed with a polyethylene spacer (large arrows) held in place by Steinman pins. This defect is then reinforced with methylmethacrylate. This procedure was developed by the senior author and is used to avoid the more complicated and increased morbidity associated with a total hip replacement. The technique of curettage and polyethylene replacement is extremely safe and reliable.

fractures of the hip require surgical reconstruction and postoperative radiation. Surgery is often warranted even in the severely weakened, nonambulatory patient; to relieve pain, to simplify nursing care, and to regain transfer ability.

Radiographs and bone scans of the femur and acetabulum must be obtained preoperatively. It is not uncommon to detect other lesions further down the shaft; a situation that indicates the need for simultaneous fixation. In general, a long-stem prosthesis will be adequate for both femoral neck and diaphyseal lesions. If the acetabulum is affected by disease, surgery should include curettage of the lesion (Figure 11.11).

Surgical Treatment

Metastatic fractures of the hip may be intracapsular (involving the femoral neck), intertrochanteric, or subtrochantic. Surgical treatment of intracapsular fractures entails endoprosthetic replacement (usually long-stem) or total hip replacement (Figures 11.12). Management of intertrochanteric and subtrochantic fractures varies;

plate and screw fixation (with PMMA) and second-generation femoral rods (with fixation extending across the femoral neck), respectively, have been described. We recommend long-stem prostheses with PMMA for metastatic involvement of any area of the hip. This is reliable and simple, avoids late failure of fixation, simultaneously treats lesions more distal in the shaft, and permits early mobilization.

Technique

A standard posterolateral approach is most often utilized. The trochanter should not be osteotomized. The head and neck are removed and the canal is reamed with *flexible* reamers (solid reamers may perforate the abnormally thin bone). The stem of the prosthesis should extend at least to the isthmus or be distal to any shaft lesions. The incision may be extended to allow resection of all gross tumor. Absent bone can be reconstructed with PMMA. It is extremely

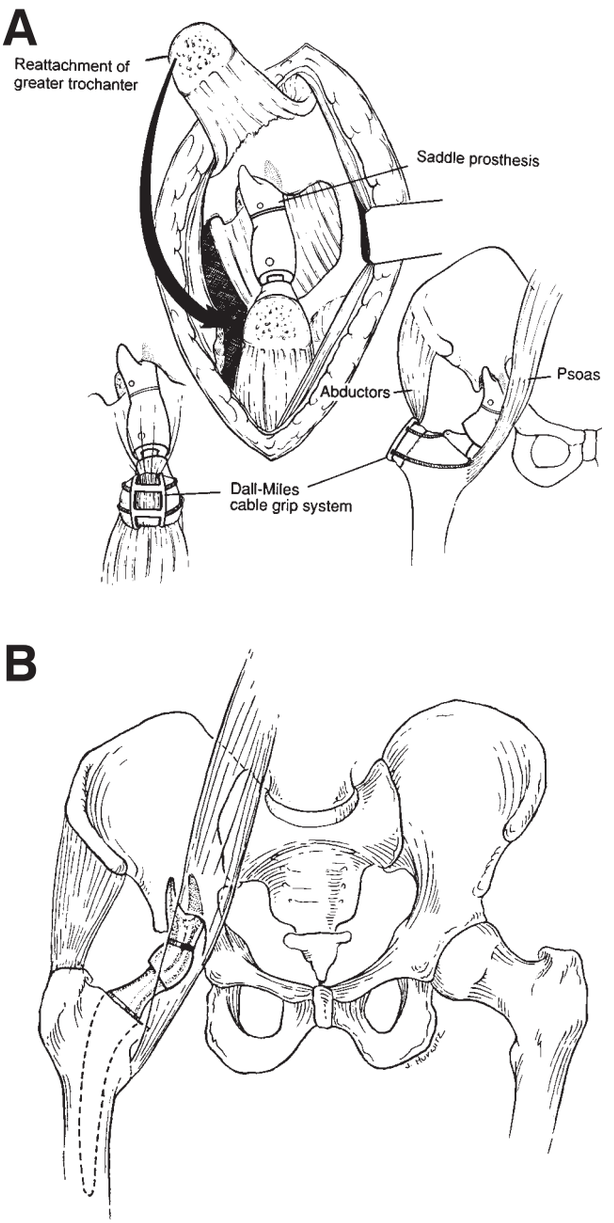

Figure 11.10 *(see above and following page).*

important to obtain a good cement mantle around the stem of the prosthesis and distal to the prosthetic tip. The PMMA should be cooled before injection to increase the time of polymerization. If loss of proximal bone loss is extensive, a segmental prosthesis is utilized. This technique can successfully reconstruct large proximal defects; however, it is associated with significant operative morbidity and not routinely performed. Postoperatively the patient is mobilized within 2–3 days; full weight-bearing on the involved extremity.

Figure 11.10 Schematic technique for saddle reconstruction of large defects of the acetabulum. The lateral approach is utilized and a trochanteric osteotomy is performed. The acetabulum is curetted and removed and is reconstructed with a femoral component with a specially designed saddle prosthesis manufactured by Link America©. The trochanter is then reattached with cables. It is important to note that the stability of this reconstruction is dependent on the abductor and psoas muscles being present and placed under the correct tension by the correct length of the body segment of the saddle prosthesis. (**B**) Schematic diagram of reconstruction following resection of a periacetabular tumor with a saddle prosthesis. *Note*: the saddle component is not fixed to the ilium but is placed in a notch such that the two horns of the saddle lie internal and external to the ilium. The femoral component is cemented into the femoral canal. This provides immediate fixation and stability equivalent to the standard total hip replacement. The major advantage of this technique is that surgical morbidity is markedly decreased when compared with a standard total hip replacement combined with a difficult reconstruction of the acetabulum which requires an oversized cup, Steinman pins and PMMA. (**C**) Saddle prosthesis (Waldermar-Link, Hamburg, Germany). This prosthesis consists of three components: femoral stem, base element (body), and the saddle component. The saddle sits in a notch made by the surgeon in the remaining ilium. The base elements are available in variable lengths. (**D**) Plain pelvic radiograph showing a large, lytic, destructive, supra-acetabular lesion (arrows) from a long-standing myeloma. This patient was non-ambulatory for 6 months. (**E**) Postoperative photograph 1 year following resection of the tumor and reconstruction with a saddle prosthesis.

Femoral Shaft

Generally, the most appropriate means of stabilizing impending or actual pathologic fractures of the femoral shaft is second-generation IM nails with locking capabilities proximally and distally. Combined osteosynthesis (i.e. plate-and-screw fixation and PMMA) may be successful; however, it is not preferred because of the risk of fracture proximal and distal to the plate, increased operative time, and the need for more extensive surgical exposure. IM rod fixation is generally done by the "open" method, i.e. the tumor/fracture site is exposed, the tumor is curetted, PMMA is injected proximal and distal, and the IM rod is inserted. The proximal and distal fragments are reamed of all gross disease to permit easy insertion of the PMMA and rod. A uniform cement mantle should be obtained around the rod. The need to open and visualize the tumor and augment it with PMMA is dependent on the size and

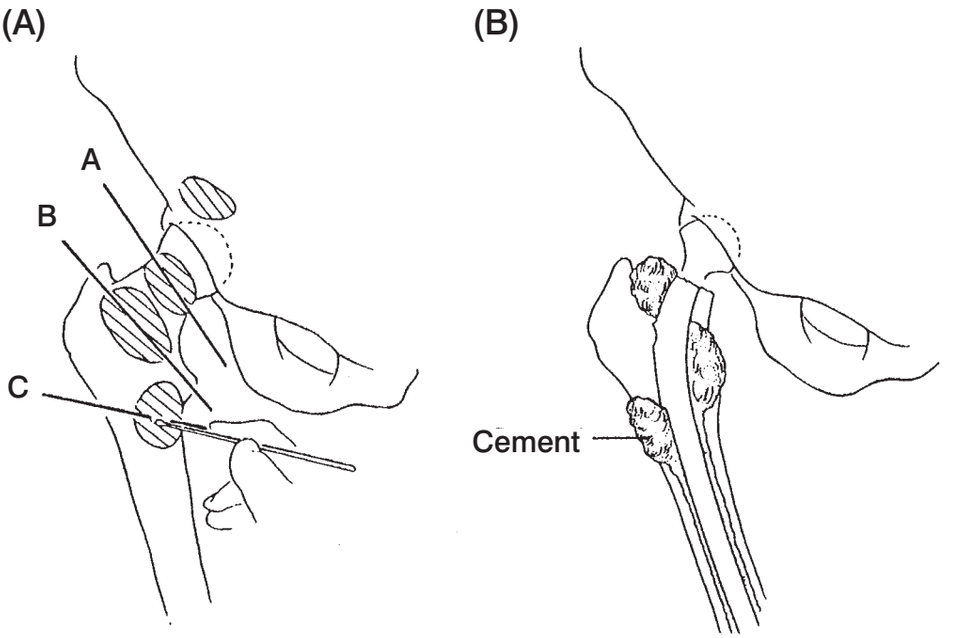

Figure 11.11 **A**: Schematic diagram of the technique of acetabular preservation for supra-acetabular metastatic tumors. The tumor is curetted out a lateral approach. (**B**) The defect is reconstructed with PMMA, Steinman pins, and a polyethylene block to support the subchondral bone. This technique has been used by the senior author to avoid a more complicated total hip replacement.

degree of cortical destruction. Immediate ambulation with full weight-bearing is permitted within a few days after surgery. Pain relief is almost universal and approximately 90% of patients maintain ambulation.

Prophylactic Femoral Shaft Fixation

Small lesions of the femoral shaft may be treated prior to fracture by the "closed" method; that is, fluoroscopically inserting an IM rod from a small incision at the tip of the greater trochanter and anterograding it through the lesion to obtain good distal fixation. When utilizing this procedure it is difficult to insert PMMA, and this method is therefore indicated only for small lesions of the femoral shaft with normal proximal bone. Careful preoperative evaluation of the hip is required, because subsequent treatment of an undetected hip lesion is extremely difficult once an IM rod is in place.

Supracondylar Femoral Fixation

Metastatic lesions of the distal femoral diaphysis and condyles are best treated by medial and lateral Zickel rods with PMMA. Large distal femoral metaphyseal lesions, especially those associated with intra-articular extension and/or large soft-tissue components, are best treated with a custom or modular distal femoral endoprosthetic replacement.

Humerus

Surgical stabilization is recommended for patients at risk for fracture and in whom stable fixation can be assured. It is also recommended to permit crutch/walker use in patients with concomitant lower extremity lesions. Large lesions, or those with a pathologic fracture, are best treated by curettage, intramedullary fixation, and PMMA. Treatment options for the proximal humerus (metaphysis, surgical neck and head) include stabilization with plate and screws or IM rods supplemented with PMMA and conventional or custom head and long-stem endoprosthetic replacement. Proximal humeral lesions are approached through a standard deltopectoral incision. Tumors of the shaft may be treated with anterograde or retrograde intramedullary nailing, plate-and-screw fixation augmented with PMMA, and customized diaphyseal spacers.

Lesions of the distal humerus are a difficult therapeutic challenge. Treatment options include crossed rush rods introduced into medial and lateral epicondyles, medial and lateral column reconstruction with plate-and-screw constructs supplemented with

Figure 11.12 (**A**) Composite photograph of various sizes of total hip replacements.

PMMA, and conversion to a long-stem (humeral and ulnar) constrained elbow arthroplasty. The surgical exposure should not include olecranon osteotomy because of the likelihood of nonunion with postoperative radiotherapy.

Lesions Distal to the Knee and Elbow

The most common primary cancers associated with distal metastases are those of the lung, kidney, breast, and gastrointestinal tract. Tumors of the forearm or tibia are best treated by IM fixation with supplemental PMMA. Tumors of the hand often require amputation. Substantial experience with extremity preservation has been accumulated with multimodality therapy for primary sarcomas of the hand and foot; however, this experience often does not apply to the management of metastases at these sites. Radiation should be used for attempted palliation in patients with metastatic disease to the hand or foot. Amputation may be used for patients who do not respond to radiotherapy.

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