PREFACE

This document sets out a statement of good practice in the Orthopaedic and Neurosurgical management of patients with metastatic bone disease.

It represents a consensus statement from the British Orthopaedic Association and the British Orthopaedic Oncology Society. Recommendations are made as to best practice standards of care.

It is hoped that this guide, which is an updated statement, will inform Surgeons, Trusts and Commissioners and further improve the care of patients with bone metastases.

ROGER M TILLMAN     ROBERT U ASHFORD

CO-CHAIRMEN BOA/BOOS WORKING PARTY
Members of the Working Party

The Appendicular Skeleton

Roger Tillman FRCS(Orth). Consultant Orthopaedic Surgeon,
Royal Orthopaedic Hospital Birmingham. (Co-Chairman, Appendicular Group).

Rob Ashford MD FRCS (Tr. & Orth). Consultant Orthopaedic Surgeon
University Hospitals of Leicester. (Co-Chairman, Appendicular Group).

Tim Briggs MD FRCS. Consultant Orthopaedic Surgeon,
Royal National Orthopaedic Hospital, Stanmore.

Gill Cribb FRCS(Tr. & Orth.). Consultant Orthopaedic Surgeon
Robert Jones & Agnes Hunt Orthopaedic Hospital, Oswestry.

Craig Gerrand MD FRCS(Tr. & Orth.). Consultant Orthopaedic Surgeon,
Freeman Hospital, Newcastle.

Jonathan Gregory FRCS(Tr. & Orth.), Consultant Orthopaedic Surgeon
Manchester Royal Infirmary

Duncan Whitwell FRCS(Tr. & Orth.) Consultant Orthopaedic Surgeon
Nuffield Orthopaedic Hospital, Oxford.
The Spine

Birender Balain FRCS(Tr. & Orth.) Consultant Spinal Surgeon,
Robert Jones & Agnes Hunt Orthopaedic Hospital, Oswestry.

Special Advisors to the Working Party

Robert E. Coleman PhD, FRCP, YCR Professor of Medical Oncology
Weston Park Hospital, Sheffield.

Claire P. Esler MRCP FRCR, Consultant Clinical Oncologist
University Hospitals of Leicester.

Janette Gross FRCA FANZCA, Consultant Anaesthetist,
University Hospitals of Leicester.
Sections

Key Points

1. Introduction
2. Evidence Level
3. Cost Benefit of Surgery for MBD.
4. Presentation to the Orthopaedic Surgeon.
5. The Role of the Orthopaedic Surgeon.
6. When is Biopsy Necessary?
7. Aims of Surgery.
8. Adjuvant Therapy.
10. Mechanism of Fracture.
11. Pre-Operative Assessment.
13. Surgical Treatment: Pelvis & Acetabulum
15. Hospital Facilities Required for the Treatment of MBD
17. Table 1. Mirel's Scoring System.
18. References.
Key Points

Infrastructure

- Each orthopaedic &/or trauma service requires a lead clinician for Metastatic Bone Disease (MBD).

Diagnosis

- There is no rush to fix a pathological fracture. Traction or splintage will suffice while investigations are performed and surgical intervention discussed with the lead clinician for MBD, the managing oncologist and other appropriate colleagues. Imaging should however be performed without delay.
- Never assume that a solitary bone lesion is a metastasis – a biopsy is necessary

Prognosis

- The prognosis for patients with MBD continues to improve. Survival in excess of 5 years is not uncommon.

Treatment

- Orthopaedic treatment should be part of a multi-disciplinary approach to management. A longer life expectancy requires a more durable reconstruction
- Fractures caused by MBD may not unite, especially if given radiotherapy. Surgical treatment should take account of this fact by, for example,
replacing bone rather than attempting fixation.

- Prophylactic fixation of long bone metastases is generally easier for the surgeon and less traumatic for the patient. Use the Mirels’ scoring system to predict those at risk of pathological fracture.
- Fixations of pathological fractures or lytic metastases, especially around the hip and proximal femur have a high failure rate. Cemented hip prostheses (either standard or tumour prostheses) have a lower failure rate. There is an evolving role for endoprosthetic replacement of the proximal femur.
- When surgery is indicated for spinal metastases, both decompression and stabilization are generally required.
- Constructs, whether spinal or appendicular, should allow immediate weightbearing and aim to last the lifetime of the patient.
- Solitary metastases (especially renal and thyroid) should, where possible, be radically excised.
- Post-operative radiotherapy should be considered in all cases except en bloc excision
- Non-surgical oncological treatment has both an established and an evolving role (bisphosphonates, radiotherapy, radiofrequency ablation & cementoplasty)
- Patients should be followed up for fixation failure if they remain well.

Ongoing pain equals disease progression or impending implant failure.
Minimum Standards of Care

• All patients should be discussed with the lead clinician for MBD

• An up to date oncologic opinion should be sought before surgical intervention

• Follow up after surgical management of metastatic bone disease should include evaluation of fracture union, local disease progression and impending or actual implant failure

• We recommend that data be collected on all skeletal metastases treated by, or referred for possible treatment by, orthopaedic surgeons. This dataset should include primary diagnosis, surgical treatment undertaken or considered, complications and outcome. Only by recognising the input of orthopaedic surgeons can the necessary funds be accessed to support such treatment, and outcomes be assessed.
1. INTRODUCTION.

1.1 This document is a consensus statement reflecting good practice in the orthopaedic management of patients with metastatic bone disease (MBD) and is approved and supported by the British Orthopaedic Association and the British Orthopaedic Oncology Society.

1.2 The incidence of MBD is difficult to determine accurately. Skeletal metastases may develop in two-thirds of cancer patients. Of the 11500 deaths in the UK from breast cancer each year, 70% have bone metastases. With a median survival of 2 to 3 years from development of bone metastases this gives a prevalence of 16-24,000 [Cancer Research UK 2012]. A recent study in the US estimated a prevalence of approximately 280,000 adults with metastatic bone disease [Li 2012], although cancer statistics support a figure of nearer 400,000 [Greenlee 2001, Coleman 2008]. Tumours which metastasise to bone most frequently are prostate, breast and kidney, followed by lung and thyroid.

1.3 Bone metastases are frequently the most symptomatic and disabling manifestation of secondary cancer, and it is essential to define adequate levels of service provision and appropriate funding in order to provide good quality clinical care.

1.4 Despite the advances in both orthopaedic oncology and spinal surgery, there remains a relatively low level of awareness in the hospital and primary care settings of what can be achieved. A review of patients with breast carcinoma by Galasko documented that in only 45 of 207 patients with painful skeletal metastases and in only 6 of 51 patients with spinal instability was an orthopaedic opinion sought [Galasko 2000]. A similar review by O'Donoghue
documented that in only half the instances where orthopaedic review would have been indicated was this undertaken and in only half of those in whom spinal surgery may have been beneficial was this undertaken [O'Donaghue 1997, Cumming 2009].

1.5 Studies and clinical experience suggest that there is a significant variation in the standard of management of patients with MBD and the surgical techniques and implants used. Poor outcomes, where they occur, can be due to a variety of reasons including the following:

a. Failure to intervene prophylactically where appropriate.

b. The use of inappropriate surgical implants, more suited to standard trauma, where fracture union can be anticipated, unlike in the management of metastatic bone disease, which leads to high failure rates [Wedin 1999].

c. Failure to appreciate the options available, particularly in more advanced cases of MBD with appropriate opinions not being obtained [Healey 2000].

Currently, there is a lack of auditable standards for the treatment of MBD and we would support therefore propose four such standards (see key points).

1.6 From available data, this document identifies the best practice in general terms and the emphasis is therefore on process rather than precise techniques. It does not attempt to define the surgical procedures applicable to any specific patient or in all circumstances. Each orthopaedic specialist must take fully into account the individual circumstances and requirements of each patient.
1.7 The prognosis for many patients with MBD, and particularly those without visceral disease, has significantly improved in recent years due principally to advances in medical therapy including hormonal treatment, bisphosphonates, chemotherapy and biologically targeted agents [Wilkinson 2008,]. In the 1970s the average survival following recognition of bone metastases was 7 months. By 1990 this had increased to 2 years. This improvement has been most marked in breast and prostate cancer, and of these, breast cancer provides the great majority of cases which merit orthopaedic intervention due to the frequency of metastatic bone lesions. This improvement places an increased burden of responsibility on orthopaedic surgeons treating MBD or who encounter MBD during the general trauma take.

1.8 This document should be read in conjunction with ‘The British Association of Surgical Oncology Guidelines for the Management of Metastatic Bone Disease in the UK’ [British Association of Surgical Oncology 1999], which gives additional information with regard to nonsurgical aspects of treatment and the NICE guidelines on metastatic spinal cord compression [NICE 2008].
2. EVIDENCE LEVEL.

2.1 This is a subject where there has, until recently, been a relative paucity of reliable scientific data. Controlled prospective trials of different treatments for MBD are difficult to construct. Despite this we consider that a sufficient volume of data and clinical experience exists to regard this guide as an evidence-based approach to MBD.

2.2 There is very little randomised controlled trial evidence for surgical intervention, most studies being retrospective case series or individual case reports.

2.3 There is increasing evidence that the use of conventional trauma implants are associated with an increased failure rate particularly in the proximal femur [Steensma 2012, Harvey 2012].

2.4 There is additional evidence that endoprosthesis replacement of the proximal femur has an evolving role in MBD [Chandrasekar 2008, Ashford 2010].
3. COST BENEFIT OF SURGERY FOR MBD.

3.1 The prompt and appropriate surgical management of skeletal metastases along the lines of the principles detailed in this guide is highly cost-effective in terms of the overall management of cancer patients. The cost of even specialised implants is recouped if a previously immobile patient is enabled to walk and live independently. The cost of an endoprosthetic replacement has been estimated at £18,000 [Ashford 2010]. The cost of treating pathological fractures in the community has been estimated at £4000 per month [Ross 2004].

3.2 There is, however, no doubt that providing an excellent service for patients with MBD places extra demands on trauma, elective orthopaedic and spinal services. This burden must be recognised by health care managers and purchasers, as should the fact that expedient treatment may lead to savings in nursing and community care costs and that reallocation of resources might be appropriate.

3.3 Inadequate orthopaedic treatment or treatment with inappropriate implants, frequently leads to complex revision surgery, causing suffering, prolonged inpatient stays and potential complications in addition to the financial cost.
4. PRESENTATION TO THE ORTHOPAEDIC SURGEON.

4.1 This is typically in one of three modes:

a. acute admission with pathological fracture or neurological compromise

b. referral from oncologist/surgical oncology team (surgeon, radiologist or oncologist).

c. referral to clinic with unexplained musculoskeletal pain

The presentation of one of the sequelae of MBD may be the first manifestation of malignancy.

4.2 Pain is the most frequent clinical symptom, ranging from a dull ache to a deep intense pain that is exacerbated by weight-bearing, and is sometimes worse at night. The aetiology of this pain is not fully understood, but probably involves the release of chemical mediators of pain including substance p, prostaglandins, growth factors, bradykinin and histamine. Fracture occurring after a period of antecedent pain and a relatively low energy injury should raise the suspicion of pathological fracture.
5. THE ROLE OF THE ORTHOPAEDIC SURGEON.

5.1 The role of the orthopaedic surgeon in the management of MBD falls into four principal categories:

a) Biopsy to establish the diagnosis
   - Biopsy should be considered when there is
     - A solitary lesion
     - No known primary cancer
     - Long disease free interval
     - History of more than one previous invasive cancer
   
   Biopsy is considered further in section 6.

b) Surgical treatment of metastatic deposits for pain and to prevent fracture

c) Stabilisation or reconstruction following pathological fracture.

d) Decompression of spinal cord and nerve roots and/or stabilisation for spinal instability.

5.2 The orthopaedic surgeon will also assess appropriateness for surgery, and can help to co-ordinate care and involve other specialties as appropriate eg. pain services, palliative care.
6. WHEN IS BIOPSY NECESSARY?

6.1 Biopsy of a lesion should always be performed where there is the slightest doubt as to the underlying pathology, and in particular where there is a solitary bony lesion. Where it is clinically clear that there is disseminated malignancy then a pragmatic decision on treatment can be taken via either a bone MDT or a site-specific MDT with orthopaedic input as this will avoid delay and is in the best interests of the patient.

Any suspicious bone lesion should be subject to staging studies, with further investigations including a full clinical history and examination, routine blood tests and radiological investigations including radio-isotope bone scan, CT chest abdomen and pelvis and MRI scan of the lesion. Following this work-up, biopsy (usually percutaneous) should be carried out and then discussed at an MDT before definitive surgery is performed.

This approach will avoid so-called ‘whoops’ procedures where a specimen of histology is sent only at the time of definitive surgery (eg reamings from a nailing procedure) and it turns out that the lesion is in fact a primary sarcoma requiring radical excision, and therefore an inappropriate procedure has been performed. Intra-medullary nailing of a long bone lesion which proves to be a primary bone tumour can be a disaster, spreading tumour cells throughout the marrow cavity, and frequently precluding limb salvage surgery.

In addition, biopsy may reveal that a lesion is either benign, from a different primary or has changed its phenotype i.e. now ER negative whereas primary was ER positive or Her2 positive whereas primary was Her2 negative.
Biopsy of metastases is likely to become increasingly routine for these latter reasons even when the diagnosis seems quite likely.

6.2 Biopsy of a bone lesion should generally be carried out by an experienced surgeon, probably in a tertiary referral centre where the definitive surgery will be performed, using percutaneous biopsy instruments and under X-ray control. If biopsy is carried out by a radiologist (eg CT guided), there should be prior discussion with the surgical team, so that the creation of inappropriate biopsy tracts can be avoided. Soft tissue lesions or soft tissue extension of a bony lesion may be suitable for tru-cut biopsy under local anaesthetic in the out-patient clinic.

6.3 Patients with a suspected solitary renal metastasis should undergo biopsy as these patients have a better prognosis if the lesion is treated as a primary neoplasm and radically excised.
7. AIMS OF SURGERY.

7.1 The aims of surgery are to relieve pain and to maintain or restore function. There is some evidence that appropriate and timely treatment of metastatic bone disease can improve survival [Baloch 2000].

The general orthopaedic principles underlying the management of impending or actual pathological fractures through metastases are as follows:

a) A primary bone tumour should be excluded.
b) The procedure should provide immediate absolute stability, allowing weight bearing.
c) The surgeon must assume that the fracture may not unite.
d) The fixation should aim to last the lifetime of the patient (therefore choice of implant and an awareness of life expectancy are essential).
e) All lesions in the affected bone should be stabilised if reasonable to do so.
f) Treatments should, where possible, be appropriate for the stage of disease and general condition of the patient, and should reflect the patient’s preferences for treatment.

All patients requiring surgery must be admitted under the care of a surgeon who is on the Specialist Register. The Consultant Surgeon need not see all the patients nor carry out all procedures, but may delegate aspects of patient care to appropriate members of the team, appropriate to their skills and competence.

Patients should have the benefit of a multidisciplinary discussion of their care.
where possible. This will normally be at a site-specific MDT ideally with orthopaedic input. Where there is diagnostic doubt or complex resection or reconstruction then they should also be discussed at a sarcoma MDT. In some cases informal discussion may be appropriate, but should be documented.
8. ADJUVANT THERAPY.

8.1 Radiotherapy may be effective both on its own and in the adjuvant setting in the treatment of MBD [Hartsell 2005]. It is usually given as a single fraction for pain relief although multiple fractions may be used for a solitary metastasis or following surgical fixation. Radiotherapy can produce effective bone healing and sclerosis and can prevent pathological fracture occurring, especially in more radiosensitive cancers (myeloma, lymphoma, small cell lung cancer and breast cancer).

Radiotherapy will not cure pain of a ‘mechanical’ nature, and only 30-40% of pathological fractures will unite even after radiotherapy [Gainor 1983].

It is recommended that following surgical procedures in patients with MBD, radiotherapy to the affected bone and operative field (unless field sizes are excessive) should be considered by a clinical oncologist within the context of the site-specific multidisciplinary team [Townsend 1994,1995; Chow 2012]. Where the medullary canal has been broached or a long bone has been nailed the whole bone should be irradiated.

In the treatment of metastatic spinal cord compression, radiotherapy should be given after decompression and stabilization. In patients not fit for surgery, or with extensive disease precluding reliable mechanical stabilization, or who have a prognosis approximately less than three months, radiotherapy alone is recommended and can improve pain, mobilization and patient function.
8.2 Endocrine therapy, bisphosphonates, chemotherapy and newer cancer biological agents all have a role in the management of patients with MBD. The indications are beyond the scope of this document but should be addressed by the multi-disciplinary team.

8.3 Denosumab is a fully human monoclonal antibody that binds to RANK ligand, a protein found on osteoclasts and involved in bone breakdown. It has been shown to be more effective than zoledronic acid in preventing skeletal related events in patients with bone metastases from solid tumours (but not multiple myeloma) and recently approved by NICE for this indication [NICE Technology Appraisal Guidance 265].
9. FRACTURE RISK ASSESSMENT

9.1 The prophylactic fixation of impending pathological fractures should be considered, particularly when the risk of fracture is high. Prophylactic fixation means that the patient can be admitted on a planned basis, and is associated with lower complications and a shorter stay in hospital (Edwards 2001). Scoring systems for assessing the risk of impending fracture can be helpful, but clinicians should also consider factors such as fitness for surgery, the effectiveness and availability of conservative treatment options (eg in the upper limb), the demands of the patient and the likelihood that the lesion will respond to nonsurgical treatment (Chow 2012). The likelihood of fracture probably increases with radiotherapy treatment in the short term [Janjan 1997]

9.2 Plain radiographs are often unreliable as a measure of cortical destruction. As a rule of thumb, where 50% of a single cortex of a long bone (in any radiological view) has been destroyed, pathological fracture should be regarded as inevitable. In addition, avulsion of the lesser trochanter is an indication of imminent hip fracture. (Phillips 1998)

9.3 Permeative osteolysis is often underestimated

9.4 High resolution CT scans may provide additional information as to the extent of bone destruction

9.5 In an effort to provide a more reliable and reproducible measure of the risk of pathological fracture, Mirels devised a scoring system (Table 1) which we
regard as a useful aid to management, both for the orthopaedic surgeon, and for the breast team and oncologists monitoring patients with MBD [Mirels 1989].

For scores of nine or above consideration should be given to prophylactic fixation prior to radiotherapy being administered. Functional pain is the most important single clinical sign (Healey 2000)
10. MECHANISM OF FRACTURE.

10.1 With respect to the appendicular skeleton, the mechanism of fracture is significantly different in pathological bone when compared to ‘normal’ traumatic fractures. Bone destruction may produce a ‘stress riser’ or an ‘open section’ defect in a long bone. Low energy fracture will then occur following minor trauma or a twisting movement. Soft tissue injury is minor compared to that seen in traumatic fractures in healthy bone. A prodrome of symptomatic functional pain is often present. Weakened and demineralised bone may give rise to a gradual insufficiency fracture, rather than a single acute event. The low energy nature of these fractures means that there is usually little soft tissue injury. Therefore patients are often more comfortable once good analgesia and limb immobilization are provided which allows time for further investigation and staging.
11. PRE-OPERATIVE ASSESSMENT.

11.1 General Patient Factors Influencing Management

a. biological, as opposed to chronological, age.

b. functional ability or performance status

c. medical co-morbidities or ASA grade

d. patient motivation. Some patients may not wish to consider surgery in a palliative context, and sensitive discussion with patients and relatives is essential. In patients with a poor performance status and life expectancy, the management should be discussed with their oncologist prior to embarking on surgery. Healey [2000] recommended a minimum life expectancy for surgery of one month for a weight bearing bone and three months for a non-weight bearing bone as a general rule.

11.2 The orthopaedic surgeon needs to assess the appropriateness of any surgery. The volume of metastatic disease is important. Visceral disease may be associated with a poor prognosis. A solitary lesion from a primary with good prognosis will require a different surgical approach to bone only metastatic breast cancer which in turn will be different to a cancer with bone and visceral metastases. In some cases the metastatic load will preclude surgical fixation. In patients with metastases with a good prognosis appropriate surgical procedures with a durable reconstruction should be chosen [Hansen 2005].

11.3 It is essential that the general condition of the patient is addressed prior to surgery. A full medical history and examination is mandatory. Co-morbidities should be optimized. Assessment should pay particular attention to nutritional
state, respiratory complications of malignancy (infection, pleural effusion) and pulmonary and myocardial toxicity secondary to chemotherapy agents, (notably anthracyclines, trastuzumab, bleomycin, busulfan, mitomycin). Both the disease process and the treatment may have affected bone marrow function and clotting. A full blood count and clotting screen should be performed and advice sought on appropriate haematological and bone marrow growth factor support to minimize risks of infection and haemorrhage.

11.4 Electrolyte Imbalance including hypercalcaemia must be assessed and, if possible, corrected prior to surgery and fluid balance monitored.

11.5 Plain radiograph of the entire affected bone is a minimum requirement. Staging studies and investigations appropriate to the clinical situation should be performed. If considering an extensive reconstructive procedure systemic restaging is recommended.

11.6 Patients with a life expectancy of less than six weeks rarely gain useful benefit from major reconstructive surgery. However, an accurate prognosis cannot always be given in MBD and decisions regarding the appropriateness of surgery, or indeed any other interventions, should be discussed within the context of the multidisciplinary team and an informed patient and family.

11.7 Early liaison with the anaesthetic service is essential and important for planning analgesia in opiate tolerant patients having major surgery, perioperative management including potential for major blood loss, vascular
access and post-operative care (HDU, epidurals etc)

11.8 Pre-operative embolisation: Tumours at risk of haemorrhage (renal, thyroid and myelomatous lesions) should be considered for pre-operative embolisation [Chatziioanou 2000]. This should ideally be less than 24 hours before surgery.

11.9 Thromboembolic prophylaxis: A decision regarding which thromboprophylactic regime is appropriate needs to be made after considering the patients co-morbid conditions. It may be influenced by the results of clotting and full blood count studies. As a general rule patients with metastatic cancer undergoing surgery are at an increased risk of thromboembolic complications [Blom 2006]. Chemical and mechanical prophylaxis should be considered. Platelet function can be abnormal in patients with widespread metastatic disease and so the regime may need to be varied across the peri-operative period to minimize bleeding risk.

11.10 Appropriate analgesic use is an important part of a patient’s management. This not only improves a patient’s quality of life, but also helps to improve mobility and the chance of meaningful recovery post operatively. Patients may need high opiate doses. Referral to a palliative care team should be considered.
12. SURGICAL TREATMENT - ‘APPENDICULAR SKELETON’

12.1 Hip.

Fractures about the hip are a frequent manifestation of MBD. Management differs significantly from that of purely traumatic fractures.

- Where destruction is limited to the femoral neck or head, a cemented hemiarthroplasty or total joint replacement is recommended as a primary procedure. Long stem femoral implants should be considered when there are metastases further down the femur.

- Subtrochanteric fractures or lesions with limited bone loss in patients with limited life expectancy are best stabilised by cephalo-medullary nails with locking screws in the femoral neck. This reduces the risk of subsequent femoral neck fracture.

- Extensive subtrochanteric bone loss or patients with a good prognosis may best be managed with endoprosthetic replacement which allows early weight bearing.

- Disease beneath a hip prosthesis can be stabilized with a plate (a percutaneous locking plate is usually the best option)

- There is no role for bone grafting in the management of pathological fractures. Reconstructions should provide immediate stability and should not rely on the ability of the grafted area to heal, particularly if there has been radiotherapy or there is a risk of local recurrence.

12.2 Shoulder Girdle and Upper Limb.

Metastatic lesions or fractures of the scapula and clavicle are usually managed with radiotherapy alone. In the humeral head, significant destruction is, in most
cases, best treated by hemiarthroplasty.

Management of metastatic disease of the humerus can be challenging. Treatment must be individualised and a case can be made for curettage, cement and locking plate for most humeral lesions. An intramedullary humeral nail may be appropriate in some cases. Very distal lesions can be difficult to treat and in some cases there is a role for humeral and elbow replacement, or cast bracing and radiotherapy. In the forearm, where stresses are relatively low, plate fixation with cement augmentation can be highly effective. Locking plates in conjunction with PMMA bone cement can be a useful option in juxta-articular metastases.

12.3 Shafts of Lower Limb Long Bones (femur, tibia).

Intramedullary nailing is the procedure of choice with locking screws to give rotational stability and to prevent telescoping. Unless the metastasis is solitary, the potential spread of tumour cells within the medullary cavity by nailing is usually acceptable within the context of palliative treatment. Debulking of the tumour before instrumentation of the bone is occasionally feasible. The entire bone and operative site should be included in the post-operative radiotherapy field. Since these fractures are unlikely to unite, load bearing, rather than load sharing, devices should be used, and solid nails, of a greater diameter than may be used for purely traumatic fractures, may be considered. Packing of major bone defects with polymethylmethacrylate (PMMA) bone cement is useful in maintaining stability in some cases. All of the lesions in the affected bone should be stabilised to minimise the need for further surgery. Cephallo-medullary nails, stabilising the femoral neck, are recommended in the femur.
12.4 Endoprosthetic Surgery.

Extensive bone destruction at the metaphyses of major long bones is sometimes so great that reconstruction can only be achieved using custom or more often modular endoprostheses (sometimes called ‘megaprostheses’). This is particularly applicable in the proximal femur [Bauer 2005], but lesions of the distal femur, proximal tibia and proximal or distal humerus can also be successfully treated this way. Endoprostheses are principally used in the management of primary bone tumours, but are increasingly used in MBD. They are highly effective in maintaining function, with a low re-operation rate. Indications are extensive bone destruction, the solitary renal metastasis and perhaps the isolated metastasis with a primary tumour with a good prognosis. Other indications for endoprosthetic replacement include a poor response to non-surgical treatment, low volume disease (particularly in the femur) and aggressive bone destruction. Referral to a supra-regional centre of orthopaedic oncology should be considered, but increasingly endoprosthetic surgery can also be carried out in regional centres specialising in the management of MBD supported by local metastatic leads. There are significant cost implications to performing major reconstructive surgery for metastases but these need to be balanced against the savings to the wider health community in caring for the patient.

12.5 Amputation.

Amputation may play a role in certain circumstances. It provides reliable pain relief in a single operation. Although there is the risk of post operative phantom
pain especially if there has been significant pre-operative pain. Typically amputation is used for fungating metastases and those cases of MBD where there is significant neurovascular involvement.
13. SURGICAL TREATMENT – PELVIS & ACETABULUM

13.1 Introduction

- The pelvis is a common site of metastatic disease and can be involved in its entirety. Disease affecting the acetabulum has direct and far reaching implications for patient morbidity, quality of life and independence due to its central role in weight bearing and mobility.
- Pelvic disease not involving the acetabulum is usually treated by radiotherapy alone.
- Patients who have undergone radiotherapy to this area may occasionally suffer pain due to radiation necrosis of the femoral head or articular cartilage.
- Adjuvant and neo-adjuvant treatments such as chemotherapy, radiotherapy, hormonal therapy and bisphosphonates have been successful in managing pain and improving the quality of life in patients with pelvic metastatic disease.
- Small focal deposits in the acetabulum are increasingly treated by percutaneous cementoplasty [Maccuro 2008], especially in those patients with a poorer prognosis.
- Disease progression with bone loss and fracture remains a common scenario. This may result in a painful and undignified end to life without access to the appropriate surgical services.
- Surgical intervention should be considered in any patient with an estimated survival of more than 6 weeks and ideally achieved in a single operation. It must be remembered that some patients may survive for
many years and therefore reconstruction techniques should be chosen accordingly.

- A multi-disciplinary approach is necessary in the management of such patients, including an understanding of the specific tumour biology and close liaison with oncologists.

13.2 Principles of Surgery

The general principles of surgical treatment are:-

- Debulking as much tumour as possible
- Filling or structurally bypassing the defect created by the tumour transferring forces proximally to intact ilium or sacrum
- Creating a durable joint reconstruction upon which the patient can fully weight bear. This may incorporate one or any combination of cement, augmentation rings, transpelvic columnar Steinmann pins and tumour prostheses for wide resections. Adopting a 'biological' approach to reconstruction is not a priority in metastatic disease.

13.3 Preoperative Assessment

Anaesthetists must be informed of potential high blood losses so that appropriate intra-operative monitoring can be established. Metastases from renal, thyroid, liver and myeloma primaries are known to bleed excessively due to their increased vascularity and preoperative embolisation is indicated in these
cases via vascular interventional radiologists. Care must specifically be noted in patients with metastatic renal cell carcinoma undergoing embolisation. Many have had previous nephrectomy as initial treatment and are thus reliant on a single functioning kidney.

Preoperative surgical planning is essential prior to undertaking reconstructive surgery in patients with metastatic disease. CT scanning is an excellent modality for assessing cortical and cancellous invasion and defines bone defects in axial, coronal and sagittal planes. MRI is more useful in delineating soft tissue components in association with metastatic deposits. It is particularly useful in assessing renal cell metastases and metastatic marrow extension of disease.

Intraoperatively, surgeons must be prepared for and competent in the management of bleeding. Ligaclips, surgical ties, diathermy, radiofrequency tissue sealing systems and adrenaline-soaked swabs may all prove useful adjuncts.

13.4 Classification of Periacetabular Defects & Appropriate Reconstruction Techniques

The Harrington Classification is a four-grade system which is most widely employed to describe acetabular defects associated with metastatic disease.
Type I defects are characterized by an acetabulum with intact anterior and posterior columns, superior dome and medial wall with only punctuate disease of the floor of the acetabulum.

These lesions uncommonly present for surgical intervention. Careful curettage of the metastatic tumour is required and occasionally ‘prophylactic’ medial wall mesh augmentation is required. Definitive reconstruction is with a standard cemented total hip replacement. Cement provides immediate stability and had the theoretical advantage of a thermonecrotic effect on tumour tissue.

Type II defects are characterized by a loss of medial wall with potential for true migration of the femoral head medially into the pelvic cavity.

After removal of tumour the principle of surgery is to reconstruct and thus protect the medial wall from further protrusion and if feasible restore the normal hip centre. This can be achieved with mesh or anti-protrusio cages depending on the defect severity. Anti-protrusio cages necessitate good exposure to ensure that during initial cementation that the ischial flange is intimately seated, and the superior iliac flanges exposed sufficiently well to facilitate screw insertion. A polyethylene liner is then cemented into the cage.
**Type III** defects are the most challenging because of defects that involves the medial wall, lateral margin and superior dome of the acetabulum. One or both columns are often involved.

These are the most difficult defects to address and represent a spectrum from intermediate to severe loss of native bone stock. Defects at the less severe end of the spectrum can be managed as previously detailed above.

Where medial defects are more extensive the Harrington technique provides an excellent solution which biomechanically facilitates the transfer of stresses across the defect from acetabulum to strong proximal bone. As above the medial defect is meshed and threaded Steinmann pins passed from the iliac crest into the acetabulum bridging the defect. Wires placed anteriorly on the iliac crest can be directed posteriorly into the acetabulum and secured within the ischiun. Similarly, pins with a more posterior entry point on the iliac crest can be directed anteriorly into the pubis creating a lattice deep to and above the level of the true acetabulum to provide support for an anti-protrusio cage which is implanted as documented above.

Simply filling such defects with cement will result in medialisation of the ‘cementoma’ due to lack of structural support. This then necessitates further complex revision surgery emphasizing the importance of adequate preoperative planning.
**Type IV** defects are rare and were originally classified as solitary lesions that were amenable to en-bloc resection.

Such defects utilize techniques such as strut or vascularised fibular graft augmentation as well as custom prostheses, saddle prostheses and more recently ice-cream cone prostheses. Such cases should be undertaken by dedicated orthopaedic oncology surgeons.

13.5 Summary

Periacetabular metastatic disease is common and the source of great morbidity in a population that is increasing in size. A more interventional approach is required to give this patient group an improved quality of life. Optimal treatment should be directed by dedicated multi-disciplinary teams and surgical intervention undertaken by those surgeons with the aforementioned techniques within their armamentarium. In addition, networks should be developed with lines of communication such that surgeons without this training have clear and timely referral pathways.

Pelvic metastatic disease can be 'silent' until significant bone loss has occurred. Therefore all clinicians involved in the care of these patients should be mindful of any symptoms, even minor ones, around the hip and pelvis. Delay in diagnosis can render pelvic and acetabular metastases inoperable.
14. **SURGICAL TREATMENT - SPINE.**

NICE guidelines have recently been published regarding the management of metastatic spinal cord compression.

14.1 Incidence

The spine is the commonest site for MBD and whilst not all spinal metastases are symptomatic, pain from the expanding tumor tissue and/or a pathological fracture, is frequently disabling. Paresis or paralysis may be the presenting feature. Untreated, high levels of dependency result, with high human and financial costs.

14.2 Background

Historically, surgical management of spinal MBD has been widely considered inappropriate due to poor outcomes for surgical and oncological reasons. Decompressive laminectomy in the presence of anterior column deficiency frequently led to further destabilisation and early instrumentation had significant design faults.

14.3 Recent Improvements

Over the last two decades there has been considerable improvement in the implants available to manage structural deficiency of the spine, notably pedicle screws, cages, cement augmentation techniques and minimally invasive spine fixation techniques. Even in the hospital sector, there remains a low level of awareness regarding spinal reconstruction techniques. A consultant spinal surgical opinion should be obtained before spinal surgical intervention is dismissed, especially before considering radiotherapy treatment to the spine. A randomised controlled trial demonstrated superior outcomes of decompressive surgery plus post-operative radiotherapy to radiotherapy alone for spinal cord
compression caused by metastatic cancer [Patchell 2005].

14.4 Presentation

This is generally in one or more of the following ways:

a. Back pain in isolation.

Worsening severity of pain not dissimilar to previously experienced degenerative spinal pain or a de novo pain of mechanical origin (from a pathological fracture or collapse) may be the presenting feature. In either case, a careful neurological examination must be performed. These patients should be nursed flat and appropriate investigations and referrals arranged. The investigation of choice for suspected spinal metastasis is a whole spine MRI, which not only is a sensitive way to pick up sites of spinal metastasis, but also helps to exclude asymptomatic spinal cord compression.

b. Incipient Neurological Compromise

All patients with partial neurological deficit should be assumed to be at risk of sudden deterioration. These patients should be nursed flat in neutral alignment, log rolled every 2-3 hours and corticosteroids and measures for thromboprophylaxis should be started. Whole spine MRI should be performed urgently. These patients should be urgently referred to a Spinal Surgeon/Unit capable of assessing and treating these lesions within 24 hours.

c. Complete Neurological Deficit

If gradual in onset and within hours of becoming complete, surgery should be considered. If rapid in onset or with complete deficit of more than 24 hours’ duration, the probability of significant recovery, particularly in the elderly, is low.

N.B. Despite complete neurological deficit, the presence of severe mechanical
pain indicates consideration of surgery. If life expectancy is less than 3 months, then provision of external support by suitable devices/orthosis would be helpful.

14.5 Patient Factors Influencing Management

a. biological, as opposed to chronological, age.
b. functional ability or performance status
c. medical co-morbidities or ASA grade
d. patient motivation. Some patients may not wish to consider surgery in a palliative context, and sensitive discussion with patients and relatives is essential. In patients with a poor performance status and life expectancy, the management should be discussed with their oncologist prior to embarking on surgery.

14.6 Spinal Factors Influencing Management

a. whether metastatic cord compression is due to tumour in isolation or due to vertebral collapse needs to be established. If structural stability is compromised, radiotherapy will be ineffective, and surgery may be the only option for neurological improvement.
b. extent of spinal involvement. This can only be adequately established with whole spine MRI
c. level and direction of compression. This is important for surgical planning.
d. duration and degree of neurological compromise. Complete paraplegia or tetraplegia for more than 24 hours should be discussed prior to transfer as surgery is unlikely to be of benefit.

14.7 Tumour Factors Influencing Management

a. Primary tumour type. Vascularity of metastasis from kidney and thyroid
should be kept in mind. Knowledge about survival rates for different primary tumors once they have metastasized to the spine would help guide appropriate management.

b. Adjuvant sensitivity to chemotherapy, radiotherapy or hormonal manipulation.

c. Staging. Isolated spinal metastases are uncommon.

14.8 Clinical Assessment.

A complete history and examination with particular attention to neurological status is mandatory. Fluid balance charts to monitor sphincter function and neurological charts are required.

14.9 Laboratory Investigations

In addition to standard haematological and biochemical analysis for any skeletal metastasis, the coagulation profile is essential. Site-dependent tumour markers may also be valuable, but their role is beyond the scope of this document.

14.10 Imaging Requirements

Plain radiographs of spine

MRI - Whole spine with sagittal T1, T2 and STIR sequences as well as axial sections through areas of interest.

Chest X Ray

_Chest CT_

_Abdominal imaging (CT or US)_

_Isotope bone scan_

(Those in italics represent desirable staging investigations, but should not delay appropriate surgical intervention if neurology is deteriorating and need
not be repeated if performed in the previous 4-6 weeks).

14.11 Biopsy of Spinal Lesions

General principles are as for non spinal tumours. Biopsy of an apparently solitary lesion should not be undertaken without prior discussion with a spinal centre. Biopsy generally requires imaging control in the form of CT or biplanar image intensifier, and should normally be performed by trephine. Multiple samples should be obtained, particularly with blastic lesions, in view of the difficulty in obtaining diagnostic material.


A number have been reported and some validated as clinically useful. Revised Tokuahsi score, Tomita score and Modified Bauer’s score are the most widely used. Their use is recommended but no system has been universally adopted.

14.13 Treatment Selection

Definitive treatment should be undertaken less than 24 hours after onset of neurological compromise, and prior to further deterioration. It should be done within 7 days in cases of mechanical instability without neurological deficit.

a. Indications for Radiotherapy

No spinal instability
Radiosensitive tumour
Stable or slowly progressive neurology
Multi-level disease
Surgery precluded by general condition
Poor prognosis
Post operative adjuvant treatment
Greater than 24 hours from onset of cord compression
Contraindicated for patients with tumors completely encircling the cord, unless surgery has been declined.

b. Indications for Surgery

Spinal instability evidenced by pathological fracture, progressive deformity, and/or neurological deficit
Clinically significant neurological compression.
Tumour insensitive to radiotherapy, chemotherapy or hormonal manipulation
Patients who have reached spinal cord tolerance after prior radiotherapy
Intractable pain unresponsive to nonoperative measures (eg radiotherapy, chemotherapy or hormonal manipulation.)
Metastasis completely encircling the cord

14.14 Objectives of Surgery

a. Prevention of further neurological deficit. Recovery of neurological deficit can occur, but is uncommon.
b. Restoration of spinal stability

Technical considerations are:

a. decompression of spinal cord and spinal nerves
b. restoration of structural integrity and stability of the vertebral column
c. feasibility of tumour eradication


Surgery should be undertaken ideally before the patient loses the ability to walk and should be done to maximize useful function.
a. The magnitude of the procedure should not exceed the patient’s ability to survive it or the surgeon’s level of competence. The surgeon requires familiarity with anterior and posterior approaches to all spinal levels. Junctional areas may require specialised approaches.
b. All constructs will eventually fail unless replaced by living tissue. If the prognosis exceeds twelve months, stronger fixation or adjunctive fusion should be considered.
c. Implants should provide immediate stability
d. Ideally, either anterior or posterior constructs alone should be sufficient to provide decompression and stability
e. Surgical implants should be made from titanium for MRI compatibility
f. Posterior constructs should be based on pedicle screw constructs with cross links for maximum stability
g. An adequate range of implants for posterior and anterior reconstruction at all levels should be available in-house
h. Radical en-bloc excision of metastatic tumours is indicated only in rare circumstances

14.16 Theatre Requirements for Spinal MBD
a. Recognition of the surgical priority of these cases and displacement of other less pressing cases when necessary.
b. Surgery during normal hours with full support, including appropriately trained theatre staff.
c. Spinal operating table permitting biplanar imaging, and trained radiographers.

14.17 Anaesthesia Requirements
a. Consultant Anaesthetist

b. Multimodal management of acute-on-chronic pain problems, including use of regional techniques where appropriate, and recognition of increased requirements for peri-operative analgesia as a result of factors such as opioid tolerance and liver enzyme induction.

c. Invasive monitoring and readiness to manage major haemorrhage, especially with respect to very vascular renal metastases.

d. Ability to provide one lung ventilation if required for spinal procedures

14.18 Post Operative Requirements

a. High Dependency Unit (HDU) facilities are mandatory. If it is anticipated that patients will require ITU facilities in terms of their general condition then it is questionable whether they should be undergoing surgery for this indication.

b. Physiotherapy and hydrotherapy are particularly desirable in assisting mobilisation and recovery following spinal procedures.

c. Thromboprophylaxis assessment, continence management and pressure area care are an important part of patient management.
15. HOSPITAL FACILITIES REQUIRED FOR THE SURGICAL MANAGEMENT OF MBD.

15.1 Facilities should include a dedicated orthopaedic ward, consultant-led trauma or elective theatre lists, laminar flow theatres and an adequate inventory of trauma, spinal and arthroplasty implants.

15.2 A skilled and prompt pathology service allowing complete haematologic and metabolic evaluations

15.3 Anaesthetists familiar with the complexity of the surgical management of patients with MBD, including the management of bleeding, fat or tumour embolus and the metabolic disturbances commonly associated with MBD.

15.4 Radiology service allowing provision of a range of different imaging modalities that can help establish the diagnosis and extent of MBD.

15.5 Specialist nurses that can help patients diagnosed with MDT, coordinate their care and attend to issues raised both clinical and psychological.

15.6 Access to appropriate MDT discussions
16. SERVICE DELIVERY AND THE MULTI-DISCIPLINARY TEAM.

16.1 The Chief Medical Officer has instructed that cancer care in England and Wales should be concentrated in Cancer Centres and Cancer Units in order to improve outcomes. The management of MBD requires input from a wide range of specialists, including surgeons, histopathologists, radiologists, clinical and medical oncologists, palliative care specialists, cancer nurses and pain specialists.

16.2 Orthopaedic surgical input to these multi-disciplinary teams is essential in order to ensure optimum care for patients with MBD.

16.3 A lead orthopaedic surgeon for appendicular MBD should be designated in each trauma group as an integral part of the multidisciplinary team. The skills of the named individual need to be maintained by CPD and this added burden must be acknowledged by Trusts. Where workload is significant, a sessional commitment may be required.

16.4 The lead orthopaedic surgeon for MBD will not, in most cases, be skilled in all aspects of trauma, arthroplasty and spinal surgery, but will be adequately trained in terms of diagnosing, investigating and coordinating the care of patients with MBD. Where appropriate this will involve liaising with a network of colleagues and regional or supra-regional centres to optimise the management of more complex cases.

16.5 Within each Health Region, clear definition of those responsible for the provision of reconstructive spinal surgery for MBD is required. The relative contribution of orthopaedic spinal surgeons and neurosurgeons will be determined at local level.

16.6 A regular weekly conference is the most appropriate vehicle for contact
between radiologists, histopathologists, oncologists, surgeons, specialist nurses and palliative care physicians. A designated individual, ideally of a nursing background should act as coordinator between the different members of the MDT to ensure that follow up of individual cases is efficient and timely. A weekly combined clinic between oncologists and orthopaedic surgeons specifically for patients with bone pain or known MBD may be a satisfactory alternative in these cases that an MDT meeting is not available. Access to an orthopaedic opinion is widely perceived to be inadequate, and without a regular clinic or conference, we consider that care of patients with MBD will be haphazard and potentially inadequate not meeting the high standards of care expected.

16.7 As current therapies for management of MBD are non-curative, improved quality of life must be a major goal. Appropriate audit of referral, medical and surgical treatment and outcomes should be compiled and made available for national comparison. Details of those in whom no intervention is undertaken and the reasons for this should be included. Data on surgically treated skeletal metastases should be maintained. The NJR currently does not list tumour as a reason for joint replacement. An appropriate patient orientated questionnaire should be introduced that will include symptom and functional scales as well as side effects of treatments, psychosocial aspects and patient expectations, in order to ensure that management of MBD whether medical or surgical never fails to primarily address and safeguard patient's quality of life. Financial and administrative support for this should be made available.

16.8 It is imperative that sufficient and timely access to the appropriate imaging facilities is made available, notwithstanding that this may mean significant alteration to current custom and practice in on-call availability. With the
recent provision of MRI facilities in most DGHs, it is no longer acceptable to transfer patients in pain and at risk of neurological deterioration to a centre for consideration of surgery only for them to be returned to the referring DGH when it has become apparent there is no surgical option.

16.9 Education of what can now be achieved for many of these patients remains a priority. The orthopaedic and spinal surgical community needs to inform professional colleagues, both in primary and secondary care, of the possibilities that now exist. Patients should be aware at the outset of their disease of the possibility of skeletal involvement and that this event can often be addressed effectively.

16.10 Subsequent to the original guidance there appears to be little progress in the establishment of bone metastases MDTs and clinics and no provision for adequate auditing of outcomes.
17. **TABLE 1.**

MIRELS' SCORING SYSTEM FOR METASTATIC BONE DISEASE.

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>SCORE</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>SITE</td>
<td></td>
<td>UPPER LIMB</td>
<td>LOWER LIMB</td>
<td>PERI-TROCHANTERIC</td>
</tr>
<tr>
<td>PAIN</td>
<td></td>
<td>MILD</td>
<td>MODERATE</td>
<td>FUNCTIONAL</td>
</tr>
<tr>
<td>LESION</td>
<td></td>
<td>BLASTIC</td>
<td>MIXED</td>
<td>LYTIC</td>
</tr>
<tr>
<td>SIZE*</td>
<td></td>
<td>&lt;1/3</td>
<td>1/3 - 2/3</td>
<td>&gt; 2/3</td>
</tr>
</tbody>
</table>

*As seen on plain radiograph, maximum destruction of cortex in any view.

*Maximum possible score is 12. A score of 8 equated to a fracture risk of 15%. If lesion scores 9 or above, then prophylactic fixation is recommended **prior** to radiotherapy.*
18. REFERENCES

Ashford RU, Hanna SA, Park DH, Pollock RC, Skinner JA, Briggs TWR, Cannon SR. Proximal femoral replacements for metastatic bone disease: financial implications for sarcoma units. *International Orthopedics* (2010); 34: 709-713


Chatziioannou AN, Johnson ME, Pneumaticos SG, Lawrence DD, Carrasco CH.


Department of Health. Improving outcomes in breast cancer – The research evidence.
Department of Health. Ref 539 1P 7k July 96 (05) Published by the NHS executive

Edwards SA et al. The treatment of impending and existing pathological fractures using the long gamma nail. *Injury* 2001:32(4); 299-306


Townsend PW, Rosenthal HG, Smalley SR, Cozad SC, Hassanein RE. Impact of postoperative radiation therapy and other perioperative factors on outcome after orthopedic stabilization of impending or pathologic fractures due to metastatic disease. Journal of Clinical Oncology 1994:12(11);2345-2350

