



British Orthopaedic Oncology Society

&

British Orthopaedic Association

Metastatic Bone Disease:

A Guide to Good Practice.

2015 Revision

PREFACE

This document sets out a statement of good practice in the Orthopaedic, Spinal and Neurosurgical management of patients with Metastatic Bone Disease and builds on the recommendations from the previous (2001) version.

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

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

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These guidelines are endorsed by the British Association of Surgical Oncology –
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Key Points

Infrastructure

- Every orthopaedic service should nominate a lead clinician to lead on the management of patients with 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 (where possible) and other appropriate colleagues. Imaging should however be performed without delay.
- Never assume that a solitary bone lesion is a metastasis – a biopsy may be required

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.
- Surgical management of long bone metastases, prior to fracture, is generally

easier for the surgeon and less traumatic for the patient. Mirels' scoring system may guide clinicians as to when fixation should be considered.

- Fixation 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 established role for endoprosthetic replacement of the proximal femur.
- When surgery is indicated for spinal metastases, both decompression **and** stabilisation are generally required.
- Reconstructions, whether spinal or appendicular, should allow immediate weight-bearing and aim to last the lifetime of the patient.
- Wide excision of solitary bone metastases should be considered where it is reasonable to do so, particularly if resectable metastases present several years after primary diagnosis of renal or thyroid cancer.
- Cancer patients are at increased risk of thrombo-embolism, particularly if they are rendered immobile. Appropriate mechanical and chemical prophylaxis must be considered and documented.
- Non-surgical oncological treatment has both an established and an evolving role (bisphosphonates, denosumab, systemic therapies (chemotherapy, hormone therapies and molecular agents), radiotherapy, radiofrequency ablation & cementoplasty)
- Patients should be followed up for fixation failure whilst they remain symptomatic. Ongoing pain may indicate disease progression and/or impending failure of the reconstruction.

Minimum Standards of Care

- All patients with MBD should have access to an expert orthopaedic opinion as part of multidisciplinary care
- Opinions for treatment should be discussed with the patient's oncologist and seen in the context of the underlying malignancy.
- Follow up after surgical management of metastatic bone disease should include evaluation of fracture union, local disease progression and impending or actual failure of the reconstruction.
- We recommend that data are collected about the orthopaedic management of patients with MBD in order to improve understanding of the experience of these patients, the impact of orthopaedic treatment and optimise approaches to surgical treatment. 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, the British Orthopaedic Oncology Society and the British Association of Surgical Oncology.

1.2 Population studies have demonstrated a consistent increase in 5-year survival in cancer patients [Storm 2010]. The incidence of MBD is difficult to determine accurately. Skeletal metastases may develop in two-thirds of cancer patients. Of the 11500 patients who die 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 other publications support a figure of nearer 400,000 [Greenlee 2001, Coleman 2008]. Although almost any carcinoma can metastasise to bone, those that do so most frequently are prostate, breast, renal, lung or thyroid in origin.

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'Donoghue 1997, Cumming 2009]. Bauer [2005] recognized the biggest challenge facing orthopaedic surgeons who treat MBD is the dissemination of knowledge to colleagues and oncologists.

1.5 Studies and clinical experience suggest that there is significant variation in the standard of management of patients with MBD and the surgical techniques and implants used. Despite guidelines [BOOS 2001] having been introduced over 10 years ago, mistakes in the management of patients with MBD remain commonplace [Harvie 2013]. Any of the following may lead to poor outcomes:

- a. Failure to intervene prophylactically where appropriate.
- b. The use of inappropriate surgical implants which rely on fracture union for long term durability. The failure of union commonly seen in fractures through bone metastases leads to high failure rates in such devices [Wedin 1999].
- c. Failure to appreciate the treatment options available, particularly in more advanced cases of MBD when appropriate opinions are often not obtained [Healey 2000].

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

1.6 This document attempts to define best practice for orthopaedic teams treating patients with MBD. 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. In breast cancer, from a population based study 52% of patients were alive 1 year after diagnosis of skeletal metastases and 26% 3 years after [Cetin 2015]. This improvement places an increased emphasis on the appropriate and expert management of patients with MBD by all who encounter them.

1.8 Orthopaedic Surgeons with responsibility for patients with MBD should ensure that oncologists and other multidisciplinary team members treating patients with cancer are aware of the benefits of orthopaedic surgery for patients with MBD.

1.9 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 lacking.

Our aim is to reflect the clinical consensus about best practice in the surgical management of patients with metastatic bone disease. Where possible, we have used the literature to support the conclusions in this document.

2.2 There is very little randomised controlled trial evidence for surgical intervention, most studies being retrospective case series or individual case reports. Many studies are from the Scandinavian Sarcoma Group who have the world’s largest registry of surgically treated skeletal metastases (Ratasvouri 2013).

2.3 There is evidence that the use of conventional trauma implants is associated with an

increased failure rate particularly in the proximal femur [Steensma 2012, Harvey 2012].

2.4 There is additional evidence that endoprosthetic replacement of the proximal femur is of benefit to patients with proximal femoral metastases [Chandrasekar 2008, Ashford 2010].

3. COST BENEFIT OF SURGERY FOR MBD.

3.1 The prompt and appropriate surgical management of skeletal metastases according to the principles in this guide is highly cost-effective. The cost of an endoprosthetic replacement 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 patients with 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, specialised orthopaedic oncology 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 an orthopaedic clinic with unexplained musculoskeletal pain

The presentation with 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. Establish the diagnosis of MBD

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, primary care and oncology.

5.3 In some units the Orthopaedic Surgeon will participate in a specialist bone metastases MDT or a site specific MDT.

5.4 Orthopaedic Surgeons managing patients with MBD may require support from specialist nurses, particularly if the diagnosis of MBD is a new one.

6. WHEN IS BIOPSY NECESSARY?

6.1 Biopsy of a suspicious lesion of bone should always be performed if there is doubt about the underlying pathology, and in particular where there is a solitary lesion in bone. Biopsies are not usually necessary if there is previously diagnosed disseminated malignancy in bone. In this case a pragmatic decision on treatment can be taken via either a skeletal metastases MDT or a site-specific MDT with orthopaedic input as this will avoid delay and is in the best interests of the patient.

Any patient with a suspicious solitary bone lesion should be investigated with a full clinical history and examination, followed by investigation with routine blood tests (FBC, U&E, LFT, Bone Profile, ESR / PV, CRP and tumour markers) and radiological investigations including CT chest, abdomen and pelvis, MRI scan of the lesion and isotope bone scanning. If a staging CT shows bone metastases then isotope bone scanning to assess the peripheral skeleton may be appropriate [Krammer 2013]. In some cases bone scan may be indicated even if a CT does not demonstrate skeletal metastases. Following this work-up, biopsy (usually percutaneous) should be carried out and then discussed at an MDT before definitive surgery is performed. In the event that appropriate facilities exist, when the suspicion of metastatic disease is high, biopsy and frozen section can be performed proceeding to definitive fixation during the same procedure.

This approach will avoid so-called ‘whoops’ procedures where a biopsy specimen is sent only after definitive surgery (eg reamings from a nailing procedure). Such surgery is usually inappropriate for sarcoma treatment. For example, intra-medullary nailing of a primary bone tumour in a long bone is an incorrect procedure, which contaminates the whole surgical field and frequently precludes limb salvage surgery and is disastrous for the patient.

In addition, biopsy of a presumed metastasis may reveal a benign diagnosis, a different primary tumour or a change between the primary disease immunophenotype and that of

the metastasis (eg. ER or HER2 status in breast cancer) which may open up different approaches to treatment.

Biopsy of metastases is likely to become increasingly routine for these latter reasons even when the diagnosis seems quite likely (Schiavon 2013).

6.2 Biopsy of a solitary bone lesion should always be carried out in consultation with and usually by a member of a Bone Sarcoma MDT.

6.3 Bone biopsies should be performed with image guidance (fluoroscopy or CT) and with percutaneous instruments. 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.

7. AIMS OF SURGERY.

7.1 Patients with MBD have simple priorities - to remain ambulant, pain free, independent and out of hospital [Harvie 2013]. 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]. Treatment of MBD can be crucial in maintaining mobility and performance status and therefore access to other treatments such as chemotherapy.

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 will not unite.
- d. The fixation should 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. 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 Orthopaedic 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 or a specialist bone metastases MDT. Where there is diagnostic doubt discussion at a Bone Sarcoma MDT may be appropriate. In some cases informal

discussion may be appropriate, but should be documented.

8. NON-SURGICAL THERAPY.

8.1 Radiotherapy may be effective both on its own and in the adjuvant setting in the treatment of MBD [Hartsell 2005]. External beam radiotherapy (EBRT) effectively relieves pain from localised sites of skeletal metastases [Chow 2013] 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, especially in more radiosensitive cancers (myeloma, lymphoma, small cell lung, prostate 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 an intramedullary nail inserted into a long bone, the whole bone should be irradiated.

In the treatment of metastatic spinal cord compression, radiotherapy should be given after decompression and stabilisation. In patients not fit for surgery, or with extensive disease precluding reliable mechanical stabilisation, or who have a prognosis of less than three months, radiotherapy alone is recommended and can improve pain, mobilisation and patient function.

8.2 Endocrine therapy, bisphosphonates, chemotherapy and newer cancer biological agents (such as denosumab) 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]. This has been further supported by a systematic review in which denosumab was more effective than zoledronic acid in reducing the incidence of Skeletal Related Events (SRE), and delayed the time to SRE [Peddi 2013].

8.4 Percutaneous cryoablation is a safe and effective treatment to achieve local tumour control and short-term complete disease remission in patients with limited metastatic disease to the musculoskeletal system [Woodrun 2013, Nicholas Kurup 2013]. High-Intensity Focussed Ultrasound (HIFU) has also shown promising results for pain relief [Halani 2014].

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, Sharma 2007, Arvinus 2014). 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 non-surgical 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, patients are at significant risk of pathological fracture. In addition, avulsion of the lesser trochanter is an indication of imminent hip fracture. (Phillips 1998)

9.3 Permeative osteolysis on plain radiography 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 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)

9.2 Scoring systems and radiographs should be taken in conjunction with the clinical assessment. Surgical treatment in metastatic bone disease is usually palliative (except in some solitary metastases) therefore surgery where there is no pain is rarely justified given the associated risks. Careful follow up is of course necessary.

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 immobilisation 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. 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. Referral to a palliative care team can be helpful in maximising benefit from conservative treatment and can help put surgery in the context of other treatment and give a holistic view of the patient and their disease.

The Scandinavian Sarcoma Group have produced a scoring system to estimate survival after bone metastases [Ratasvuori 2013]

Score	0	1
Number of Metastases	Single	Multiple
Visceral Metastases	None	Yes
Breast / Renal / Thyroid / Myeloma	Yes	Other
Karnofsky Score >70	Above (Self caring)	Below (Needs help)

A total score of 0 or 1 is associated with two-thirds of patients surviving over 12

months. Patients with a score of 2 or 3 patients are likely to survive over 3 months and a score of 4 is associated with less than 3 months survival in 75% of cases.

11.2 The orthopaedic surgeon needs to assess the appropriateness of any surgery. The most important factors affecting survival following surgery are primary tumour, presence of organ metastases, overall health status and number of bone metastases. Patients with bone metastases arising from breast or renal primary cancers have a better prognosis than those with metastatic lung cancer.

An estimate of survival and disease load is very important in procedure and implant choice. In patients with metastases with a good prognosis appropriate surgical procedures with a durable reconstruction should be chosen. *En-bloc* resection should be considered in solitary, good prognosis metastases, especially renal. [Ratasvuori 2014,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 re-staging is

recommended.

11.6 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). Patients with active chest involvement may be at particular risk from surgical interventions involving cemented implants.

11.7 Pre-operative embolisation: Tumours at risk of haemorrhage (renal and thyroid) should be considered for pre-operative embolisation. This has been shown to significantly reduce blood loss, packed cell transfusion volume and operative time. Embolisation should ideally be performed less than 48 hours before surgery. [Chatziioanou 2000, Pazonis 2014]

11.8 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.

11.9 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.

12. SURGICAL TREATMENT - 'APPENDICULAR SKELETON'

Surgical Techniques

Surgical treatment of metastatic disease requires an individualised approach and choice of technique and implant will depend on factors already mentioned such as tumour

type, disease load and life expectancy but also on anatomical variations and co existing orthopaedic pathology such as osteoarthritis.

In general, the surgical options are either to support the bone with intramedullary nails or plates and screws augmented with cement or to replace the bone. Implant failure and periprosthetic fracture account for a significant proportion of complications requiring re-operation after surgical management of MBD [Weiss 2014]

Histological confirmation of MBD should always be obtained at surgery.

12.1 Internal Fixation

Historically internal fixation of bone metastases or fractures has had a high failure rate. Consideration should be given to the use of load bearing rather than load sharing devices. Peri-articular and other locking plates are very useful. Filling of defects with cement will add strength and therefore improve pain and function. Post operative radiotherapy may reduce recurrence rates following intralesional procedures

12.2 Endoprosthetic Surgery.

Bone destruction at the metaphyses of major long bones is sometimes so extensive that reconstruction can only be achieved using custom or more often modular endoprostheses (sometimes called ‘megaprostheses’). This is most often seen 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. Endoprosthetic replacement has been demonstrated to be an effective option in renal metastases (Hwang 2014) and also for the proximal femur (Ashford 2010). As well as 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 orthopaedic oncology centre 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 this needs to be balanced against the savings to the wider health community in caring for the patient.

12.3 Amputation.

Amputation may play a role in certain circumstances. It can provide 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.

12.4 Proximal Femur

One third of bone metastases occur in the proximal femur and as reflected in the Mirels scoring system risk of fracture is higher than in other locations. Management of metastatic fractures differs significantly from that of purely traumatic fractures. Even amongst specialist tumour surgeons there are differing opinions as to the best way to manage metastases of the proximal femur [Steensma 2013]. Particular attention should be paid to the principals that surgery must allow immediate full weight bearing and that metastatic lesions are unlikely to heal when planning operative intervention around the hip. Prognosis, site of tumour within the bone and extent of bone loss determine the appropriate management plan.

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

- *Femoral neck.* Lesions in the femoral neck are usually best managed with cemented hemiarthroplasty or total hip replacement.
- *Pertrochanteric.* In patients with a good prognosis or extensive bone loss at this site proximal femoral replacement should be considered. If prognosis is poor (eg <6 months) then cement augmented internal fixation may be appropriate if there is sufficient bone stock.
- *Subtrochanteric.* Patients with a good prognosis or with extensive subtrochanteric bone loss are often best managed with endoprosthetic replacement (Chandrasekar 2008). Metastatic deposits at this site are amongst the most frequent causes of implant failure. In patients with limited subtrochanteric bone loss with limited life expectancy may be best stabilised by cephalo-medullary nails with locking screws in the femoral neck or internally fixed with plate and screws (eg DHS) with cement augmentation.
- *Periprosthetic metastases.* Disease occurring beneath a hip prosthesis needs to be managed with careful consideration of the patients prognosis and risk of implant failure if the metastasis cannot be controlled locally. Management may consist of stabilization with a plate +/- cement augmentation or endoprosthetic replacement.
- There is no role for bone grafting in the management of appendicular 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. Cement can be useful where there are bone defects.

Evidence shows greater durability and lower re-operation rates, in the proximal femur, with endo-prosthetic replacement compared with osteosynthesis (both IM nail and plate and screw fixation) (Harvey 2012, Steensma M 2012, Wedin 2005). Surgical complications requiring re-operation occur early post-surgery (Wedin 2012)

12.5 Diaphysis of Lower Limb Long Bones (femur, tibia).

For patients with multiple metastases where there is sufficient bone stock, 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. **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. Consideration of stabilisation of all of the lesions in the affected bone to minimise the need for further surgery. Cephalo-medullary nails stabilising the femoral neck are recommended in the femur. In non-responsive tumours (such as from a renal primary) in patients with a relatively good prognosis, endoprosthetic replacement should be considered.

12.6 Distal Femur / Proximal Tibia

- *Distal femoral and proximal tibial metaphysis / periarticular lesions.* Fixation with cement augmented site specific locking plates is appropriate for most patients. If there is significant bone loss or a good prognosis then consideration can be given to distal femoral replacement . There is usually little role for endoprosthetic reconstruction of the tibia given the functional consequences and such cases should be discussed with a regional tumour centre.
- *Distal tibial metaphyseal / periarticular lesions.* This is a very challenging anatomical site. Immobilisation in plaster / supportive boot and radiotherapy may be most appropriate depending upon prognosis and the risk of operative complications at this site. Surgery usually consists of cement augmented site specific locking plate fixation. In some patients with significant bone loss

amputation may be appropriate.

12.7 Shoulder Girdle and Upper Limb.

- *Scapula and Clavicle.* Metastatic lesions or fractures of the scapula and clavicle are usually managed with radiotherapy alone.
- *Humerus.* Management of metastatic disease of the humerus can be challenging. Function is usually optimized by procedures which preserve the rotator cuff but the construct must be durable and have sufficient stability to provide pain relief. Cement augmented locking plate fixation is often the most appropriate treatment for lesions affecting the upper limb (Gregory 2011, Weiss 2011) but cast bracing and radiotherapy can be a useful treatment plan for some patients (eg. with multiple myeloma) where healing of lesions can occur.
- *Proximal humerus.* In many cases cement augmented locking plate fixation of the proximal humerus provides good stability and function. However if there is significant bone loss then arthroplasty may be considered. Traditionally this has involved hemiarthroplasty for humeral head lesions and proximal humeral replacement for metaphyseal lesions. The use of reverse polarity total shoulder replacements may improve function compared to hemiarthroplasty / standard monopolar proximal humeral replacement but more extensive surgery needs to be balanced against prognosis.
- *Diaphyseal lesions.* In patients with poor prognosis or with preservation of bone stock a locked intra-medullary nail may be appropriate. This is also useful if there is felt to be a risk of fungation if a large soft tissue mass is associated with the tumour. Curettage and cement augmentation combined with an extended metaphyseal locking plate can provide excellent stability and a durable construct when there is significant bone loss.
- *Distal Humerus.* Very distal lesions can be difficult to treat and in some cases there is a role for humeral and elbow replacement, Periarticular distal humeral locking plates with cement augmentation can be effective in the treatment of pain and preservation of function.

- *Forearm.* Plate fixation with cement augmentation is suitable for the vast majority of lesions.

12.8 Complications of Surgery

In a number of series from the Scandinavian Sarcoma Group (Wedin 1999, Wedin 2011, Weiss 2012, Weiss 2014) implant failures for internal fixation are higher than for endoprosthetic replacement (Forsberg 2013).

Patient survival does not appear to be lower after joint replacement for MBD than after other types of surgical treatment (Sorensen 2013).

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.
- Small focal, painful deposits in the acetabulum are increasingly treated by percutaneous cementoplasty [Maccauro 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.
- Patients with extensive acetabular disease may be best managed in a specialist bone tumour unit.

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. Preoperative embolisation is indicated in highly vascular metastases (eg. from renal, thyroid or liver primaries).

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 bone metastases of renal origin 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. PMMA cement can also be a useful adjunct to stop bleeding.

13.4 Classification of Periacetabular Defects & Appropriate Reconstruction

Techniques

The Harrington Classification (Harrington 1981) is a four-grade system which is most widely employed to describe acetabular defects associated with metastatic disease.

Type II - IV defects should be considered for referral to a specialist centre.

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 has 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 [Tillman 2008]. 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 ischium. 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, saddle and ice-cream cone prostheses. Such cases should usually be undertaken by dedicated orthopaedic oncology surgeons.

13.5 Complications

The complication rate of pelvic reconstructive surgery in this patient group is high and this should be considered in the appropriateness of surgery and when counselling the patient. (Issack 2013, Marco 2000)

13.6 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.

There are a number of guidelines and documents referring to the management of spinal metastases and metastatic spinal cord compression (MSCC) .

- NICE guideline GL75 (MSCC). (NICE 2008)
- NICE MSCC Quality standard QS56 2014
- DH Spinal taskforce report 2013
- Acute Oncology Measures update 2015

These are all available on or through links on the United Kingdom Spine Societies Board website (www.ukssb.com).

14.1 Incidence

The spine is the commonest site for MBD accounting for approximately 50% of bone metastases. Whilst not all spinal metastases are symptomatic, pain from the expanding tumour 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 instrumentations had significant technical limitations. 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], although entry criteria for the study were highly selective (radiosensitive tumours such as lung cancer and lymphoma were excluded). The NICE guidance for MSCC has highlighted the importance of senior multi-disciplinary involvement in patients with MSCC and care should be led by a MSCC co-ordinator which in many centres is a specialist MSCC nurse (NICE 2008). Given recent improvements in oncological control of the underlying disease many patients now live for numbers of years following the development of spinal metastasis or an episode of MSCC. The treatment strategy and if indicated the technique of spinal reconstruction therefore needs to be selected relative to the anticipated prognosis.

14.4 Presentation

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

a. Back pain in isolation.

Low back pain is a common complaint and frequently caused by other conditions which affects approximately one third of the population each year, 20% of whom visit their GP and are managed conservatively and appropriately without investigation for the most part.

Low back pain alone is non-discriminatory. Patients with cancer suffer non-specific back pain as often if not more frequently than the general population, and less than 0.1% of people who visit their GP with back pain have spinal metastases. However there are some features of pain that are better predictors of spinal cord compression such as localisation in the upper or midspine (cervical or thoracic spine), progressive discomfort, severe unremitting pain and pain aggravated by activities that increase the pressure within the spinal canal such as coughing, sneezing and defaecating. However, it is extremely difficult to exclude MSCC in any patient with known cancer who complains of localised spinal pain. Even the absence of pain does not exclude MSCC. Most patients with spinal metastases experience pain for several weeks before developing neurological symptoms and signs of MSCC. It is therefore important to

recognise that unremitting spinal pain in a patient with known malignancy requires urgent discussion and preliminary assessment by the patient's multidisciplinary cancer team or MSCC coordinator (and similarly those without a known prior cancer diagnosis but suggestive history and signs need urgent assessment to exclude a malignant cause for their symptoms). This should include a careful neurological examination. If there is a strong clinical suspicion of spinal instability or impending MSCC patients should initially be nursed flat whilst appropriate investigations and referrals are 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 measures for thromboprophylaxis considered depending on the timing of any potential surgical intervention.

Historically and in the 2008 NICE guideline steroids were recommended if there was radiological evidence of neurological compression. A recent Cochrane review however concluded beneficial effects were not significantly different with high-dose versus moderate-dose steroids or placebo, but serious adverse effects were more frequent with high-dose steroids. Currently it is suggested that these should be reserved for clinically deteriorating neurological deficit (Authors opinion and current policy)

Whole spine MRI should be performed urgently. These patients should be urgently referred to a Spinal Surgeon/Unit capable of assessment and if clinically appropriate treatment commenced 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 may justify consideration of surgery. If life expectancy is less than 3 months, then

provision of external support by suitable devices/orthosis can be helpful. A single fraction of radiotherapy can also be effective in controlling pain in patients who are paralysed.

14.5 Spinal Factors Influencing Management

- 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.
- Extent of spinal involvement. This can only be adequately established with whole spine MRI
- Level and direction of compression. This is important for surgical planning.
- 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.

14.6 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.

14.7 Imaging Requirement

- Plain radiographs of the spine should not be performed either to make or to exclude the diagnosis of spinal metastases or MSCC. Plain radiology is not as sensitive for detecting metastatic bone disease as MRI and does not readily show soft tissue abnormalities.
- MRI - Whole spine with sagittal T1, T2 and STIR sequences as well as axial sections through areas of interest
- Chest Radiograph
- *CT Chest, Abdomen and Pelvis (CT CAP)* (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).

- CT of the involved levels of the spine (normally as part of the CT CAP). should include sagittal and coronal reconstructions for the assessment of spinal stability. See SINS scoring below

14.8 Spine Scoring Systems.

A number of scoring systems have been reported and some validated as clinically useful. Revised Tokuhashi score, Tomita score and Modified Bauer's score are the most widely used. The simplest prognostic spinal scoring system is the Oswestry Spinal Risk Index (OSRI)[Balain 2013, Whitehouse 2014]. The OSRI summates primary tumour pathology and general condition. Their use is recommended but no system has been universally adopted.

The Spine Instability Neoplastic Score (SINS- appendix 2) can guide clinicians in identifying when patients with neoplastic disease of the spine may benefit from surgical consultation. It is also of assistance to surgeons in quantifying and summing structural deficiency contributing to potential spinal instability.

14.9 Treatment Selection

All cases of MSCC should be discussed with the patient's oncologist to obtain an expert opinion on prognosis. Thereafter, definitive treatment should be started, if appropriate, before any further neurological deterioration and ideally within 24 hours of the confirmed diagnosis of MSCC. Relevant investigations should be done in time to allow definitive treatment to be planned within 1 week of the suspected diagnosis in the case of spinal pain suggestive of spinal metastases, and within 24 hours in the case of spinal pain suggestive of spinal metastases and neurological symptoms or signs suggestive of MSCC, and occasionally sooner if there is a pressing clinical need for emergency surgery

a. Indications for Radiotherapy

- No spinal instability
- Radiosensitive tumour

- Stable or slowly progressive neurology
- Multi-level disease
- Surgery precluded by general condition
- Poor prognosis (< 3 months)
- Post operative adjuvant treatment
- c. Greater than 24 hours from onset of cord compression

b. Indications for Surgery

- Spinal instability evidenced by pathological fracture, progressive deformity, and/or neurological deficit
- d. 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 non-operative measures (eg. radiotherapy, chemotherapy or hormonal manipulation.)
- d. Metastasis completely encircling the cord

14.10 Objectives of Surgery

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

Technical considerations are:

- Decompression of spinal cord and spinal nerves
- Restoration of structural integrity and stability of the vertebral column
- f. Feasibility of tumour eradication

14.11 Principles of Surgery of Particular Significance in Spinal Disease.

Surgery should be undertaken ideally before the patient loses the ability to walk and

should be done to maximise useful function.

- 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.
- Implants should provide immediate stability and last the lifetime of the patient
- Ideally, either anterior or posterior constructs alone should be sufficient to provide decompression and stability
- Surgical implants should be made from titanium for MRI compatibility
- b. Posterior constructs should be based on pedicle screw constructs with cross links for maximum stability
- An adequate range of implants for posterior and anterior reconstruction at all levels should be available in-house
- e. Radical en-bloc excision of metastatic tumours is indicated only in rare circumstances

15. OUTCOMES ASSESSMENT OF SURGICAL MANAGEMENT OF MBD.

15.1 The Scandinavian Sarcoma Group have been at the forefront of data capture and outcomes assessment for many years [Ratasvuori 2013]. Publications from the group can be used as a resource to inform patients of outcomes.

15.2 In the era of surgeon reported outcomes it is desirable that units capture data on MBD. Data on patients on whom surgical treatment is deemed inappropriate should ideally be captured as well.

16. HOSPITAL FACILITIES REQUIRED FOR THE SURGICAL MANAGEMENT OF MBD.

16.1 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.

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

16.3 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.

16.4 Radiology service allowing provision of a range of different imaging modalities that can help establish the diagnosis and extent of MBD and interventional radiologists available to perform pre operative embolisation.

16.5 Specialist nurses who can help patients diagnosed with MBD, coordinate their

care and attend to issues raised both clinical and psychological. Specialist nurses are mandatory for centres managing metastatic spinal cord compression and are essential to an organised, efficient service.

16.6 Access to appropriate MDT discussions

16.7 Access to a palliative care team

17. SERVICE DELIVERY AND THE MULTI-DISCIPLINARY TEAM.

17.1 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.

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

17.3 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. This helps to concentrate experience in the management of these complex cases and provides a specific individual as a point of referral to improve the patient pathway for individuals with skeletal metastatic disease.

17.4 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. Having a named orthopaedic lead in each trust will facilitate development of a formal or informal hub and spoke service. This will allow local clinicians to be supported by regional tumour units in the provision of care for patients with metastatic bone disease. The lead MBD orthopaedic surgeon will also need to work with the metastasis of unknown primary origin team. This will allow orthopaedic input into diagnostics for patients under the unknown primary team and vice versa. Consideration should be

given to centres offering real time advice on the management of bone metastases. With IEP (Image Exchange Portal) technology and PACS (Picture Archiving and Communication Systems) available in multiple hospitals “immediate advice services” for bone metastases may become feasible.

17.5 Within health regions, 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.

17.6 It is desirable for each hospital trust or group of trusts should have a multi-disciplinary meeting for discussion of patients with metastatic bone disease. This may be a ‘virtual’ meeting consisting of dedicated time for telephone discussions or a regular weekly conference depending upon the volume of cases. In hospitals with significant trauma volumes or co-located with oncology services it is envisaged that the most appropriate vehicle for contact between radiologists, histopathologists, oncologists, surgeons, specialist nurses and palliative care physicians would be a dedicated meeting. 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. Early advice on management options for the patient with MBD should be sought, allowing earlier treatment and potentially improved outcomes.

17.7 As current therapies for management of MBD are non-curative, improved quality of life must be a major goal. The working party believes that more robust data collection is required in order to support research and service provision for patients suffering from metastatic bone disease. Local records of referrals, 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. The work of the Scandinavian Sarcoma Group on Skeletal Metastases is noted [Ratasvuori 2013] and it is recognised that there would be significant difficulties in gathering such data. Data on surgically treated skeletal metastases should be maintained. There is no current reporting of endoprotheses on the National Joint Registry although this is being piloted.

17.8 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 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.

17.9 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.

17.10 As recommended in the original guidance there remains the need for the establishment of bone metastases MDTs and clinics.

18. MIRELS' SCORING SYSTEM FOR METASTATIC BONE DISEASE.

VARIABLE SCORE	1	2	3
SITE	UPPER LIMB	LOWER LIMB	PERI-
			TROCHANTERIC
PAIN	MILD	MODERATE	FUNCTIONAL
LESION	BLASTIC	MIXED	LYTIC
SIZE*	<1/3	1/3 - 2/3	> 2/3

*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.*

19. SINS SCORE

Spine Instability Neoplastic Score

Location

- 3 points: Junctional (C0-C2, C7-T2, T11-L1, L5-S1)
- 2 points: Mobile spine (C3-C6, L2-L4)
- 1 point: Semi-rigid (T3-T10)
- 0 points: Rigid (S2-S5)

Pain relief with recumbency and/or pain with movement/loading of the spine

- 3 points: Yes
- 1 point: No (occasional pain but not mechanical)
- 0 points: Pain free lesion

Bone lesion

- 2 points: Lytic
- 1 point: Mixed (lytic/blastic)
- 0 points: Blastic

Radiographic spinal alignment

- 4 points: Subluxation / translation present
- 2 points: De novo deformity (kyphosis / scoliosis)
- 0 points: Normal alignment

Vertebral body collapse

- 3 points: >50% collapse
- 2 points: <50% collapse
- 1 point: No collapse with >50% body involved
- 0 points: None of the above

Posterolateral involvement of the spinal elements (facet, pedicle or costovertebral joint fracture or replacement with tumor)

- 3 points: Bilateral
- 1 point: Unilateral
- 0 points: None of the above
-

• Interpretation

- sum score 0-6: stable
- sum score 7-12: indeterminate (possibly impending) instability
- sum score 13-18: instability

SINS scores of 7 to 18 warrant spinal surgical consultation.

Fisher CG et al 2010

20. REFERENCES

Arvinius C, Parra, JLC, Mateo LS, Maroto RG, Borrego AF, & Stern LLD. Benefits of early intramedullary nailing in femoral metastases. *International orthopaedics* (2014); 38(1), 129-132.

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

Balain B, Jaiswal A, Trivedi JM, Eisenstein SM, Kuiper JH, Jaffray, DC The Oswestry Risk Index: An aid in the treatment of metastatic disease of the spine. *Bone & Joint Journal* (2013), 95(2), 210-216.

Bauer HC. Controversies in the management of skeletal metastases. *Journal of Bone & Joint Surgery* (2005):87-B(5);608-617

Bhamra JS, Malik AA, Aresti NA, Khan WS, Pollock R. The perioperative management of skeletal metastases *Journal of Perioperative Practice* (2012):22(1);24-29

Blom JW, Vanderschoot JPM, Oostindie r MJ, Osanto S, van der Meer FJM, Rosendaal FR. Incidence of venous thrombosis in a large cohort of 66 329 cancer patients: results of a record linkage study. *Journal of Thrombosis & Haemostasis* (2006): 4; 529–35.

British Association of Surgical Oncology. Guidelines for the Management of Metastatic Bone Disease in the United Kingdom. *European Journal of Surgical Oncology* (1999):25:3-23

British Orthopaedic Association. Metastatic bone disease: a guide to good practice, December 2001.

Cancer Research UK. Breast Cancer Mortality Statistics.

<http://www.cancerresearchuk.org/cancer-info/cancerstats/types/breast/mortality/uk-breast-cancer-mortality-statistics>

Cetin K, Christiansen CF, Sværke C, et al. Survival in patients with breast cancer with bone metastasis: a Danish population-based cohort study on the prognostic impact of initial stage of disease at breast cancer diagnosis and length of the bone metastasis-free interval. *BMJ Open* 2015;5:e007702. doi:10.1136/bmjopen-2015-007702

Chandrasekar C, Grimer RJ, Carter SR, Tillman RM, Abudu AT. Modular endoprosthetic replacement for metastatic tumours of the proximal femur
Journal of Orthopedic Surgery. 2008; 3: 50.

Chatziioannou AN, Johnson ME, Pneumaticos SG, Lawrence DD, Carrasco CH. Preoperative embolisation of bone metastases from renal cell carcinoma. *European Radiology* (2000);10:593-596

Chow, E., Khan, L. M. and Bruland, Ø. S. (2013) Radiotherapy of Skeletal Metastases, in Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, Eighth Edition (ed C. J. Rosen), John Wiley & Sons, Inc., Ames, USA.
doi: 10.1002/9781118453926.ch91

Chow E, Zeng L, Salvo N, Dennis K, Tsao M, Lutz S. Update on systematic review of palliative radiotherapy trials for bone metastases. *Clinical Oncology* (2012);24:112-124

Coleman RE, Guise TA, Lipton A et al. Advancing Treatment for Metastatic Bone Cancer. *Clinical Cancer Research*. (2008); 14(20): 6387–6395.

Cumming D, Cumming J, Vince A, Benson R. Metastatic bone disease: the requirement for improvement in a multidisciplinary approach. *International Orthopedics* 2009; 33(2): 493–496.

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

Fisher CG, DiPaola CP, Ryken TC, Bilsky MH, Shaffrey CI, Berven SH, et al. A novel classification system for spinal instability in neoplastic disease: an evidence-based approach and expert consensus from the Spine Oncology Study Group. *Spine* 2010; 35:E1221-9.

Forsberg, J. A., Sjoberg, D., Chen, Q. R., Vickers, A., & Healey, J. H. (2013). Treating metastatic disease: Which survival model is best suited for the clinic?. *Clinical Orthopaedics and Related Research*®, 471(3), 843-850.

Forsberg, J. A., Wedin, R., & Bauer, H. (2013). Which implant is best after failed treatment for pathologic femur fractures?. *Clinical Orthopaedics and Related Research*®, 471(3), 735-740.

Gainor BJ, Buchert P. Fracture Healing in Metastatic Bone Disease. *Clinical Orthopedics & Related Research* (1983); 178: 297-302

Galasko C S B. Skeletal Metastases. London. Butterworth 1986.

Galasko C S B, Norris H E, Crank S. Spinal Instability secondary to Metastatic Cancer. Current Concepts Review *Journal of Bone & Joint Surgery*(Am) 2000; 82:570-576

Gregory JJ, Ockendon M, Cribb GL, Cool PW, Williams DH. The outcome of locking plate fixation for the treatment of periarticular metastases. *Acta Orthop Belg.* 2011 Jun;77(3):362-70.

Halani, S., Coccagna, J., Chow, E., Hynynen, K., & Czarnota, G. J. (2014). High-Intensity Focussed Ultrasound and Radio-Frequency Ablation for Bone Metastasis Treatment. In *Bone Metastases* (pp. 275-300). Springer Netherlands.

Harrington K D. Orthopaedic Management of Extremity and Pelvic Lesions. *Clinical Orthopedics & Related Research* 1995; 312: 136-147

Hansen BH, Keller J, Laitinen M et al. The Scandinavian Sarcoma Group skeletal metastasis register: Survival after surgery for bone metastases in the pelvis and extremities. *Acta Orthopaedica Scandinavica* (2004):74(Suppl 311);11-15

Harrington KD. The management of acetabular insufficiency secondary to metastatic malignant disease. *J Bone Joint Surg Am.* 1981 Apr;63(4):653-64.

Hartsell WF, Scott CB, Bruner DW et al. Randomized Trial of Short- Versus Long-Course Radiotherapy for Palliation of Painful Bone Metastases. *Journal of the National Cancer Institute* (2005):97(11):798-804

Harvey N, Ahlmann ER, Allison DC, Wang L, Menendez LR. Endoprostheses Last Longer Than Intramedullary Devices in Proximal Femur Metastases. *Clinical Orthopedics & Related Research* (2012) 470:684–691

Harvie P, Whitwell D. Metastatic bone disease Have we improved after a decade of guidelines?. *Bone and Joint Research* (2013), 2(6), 96-101.

Healey JH, Brown HK. Complications of Bone Metastases: Surgical Management. *Cancer*(2000):88(12 Suppl);2940-2951

Hwang, N., Nandra, R., Grimer, R. J., Carter, S. R., Tillman, R. M., Abudu, A., & Jeys, L. M. (2014). Massive endoprosthetic replacement for bone metastases resulting from renal cell carcinoma: Factors influencing patient survival. *European Journal of Surgical Oncology (EJSO)*, 40(4), 429-434.

Janjan, NA. Radiation for bone metastases. *Cancer* (1997), 80: 1628–1645.

Issack PS, Kotwal SY, Lane JM Management of metastatic bone disease of the acetabulum. *J Am Acad Orthop Surg.* 2013 Nov;21(11):685-95. doi: 10.5435/JAAOS-21-11-685.
Review..

Krammer, J., Engel, D., Schnitzer, A., Kaiser, C. G., Dinter, D. J., Brade, J., ... & Wasser, K. (2013). Is the assessment of the central skeleton sufficient for osseous staging in breast cancer patients? A retrospective approach using bone scans. *Skeletal radiology*, 42(6), 787-791.

Maccauro G, Liuzza F, Scaramuzzo L, et al. Percutaneous acetabuloplasty for metastatic acetabular lesions. *BMC Musculoskeletal Disorders* 2008, 9:66

Malviya A, Gerrand CH. Evidence for orthopaedic surgery in the treatment of metastatic bone disease of the extremities: A review article. *Palliative Medicine* (2012):26(6);788-796

Marco RA, Sheth DS, Boland PJ, Wunder JS, Siegel JA, Healey JH. Functional and oncological outcome of acetabular reconstruction for the treatment of metastatic disease. *J Bone Joint Surg Am.* 2000 May;82(5):642-51.

Mirels H. Metastatic Disease in long bones. A proposed Scoring System for diagnosing impending pathologic fracture. *Clinical Orthopedics & Related Research* 1989: 249; 256-264

NICE guidelines for Metastatic Spinal Cord Compression: Clinical Guideline 75.
<http://www.nice.org.uk/CG75>

NICE Technology Appraisal Guidance 265 (2012). Bone metastases from solid tumours – denosumab. <http://guidance.nice.org.uk/TA265>

Nicholas Kurup, A., & Callstrom, M. R. (2013). Ablation of musculoskeletal metastases: pain palliation, fracture risk reduction, and oligometastatic disease. *Techniques in vascular and interventional radiology*, 16(4), 253-261.

O'Donoghue D S, Howell A, Walls J. Orthopaedic Management of structurally significant Bone Disease in Breast Cancer Metastases. *Journal of Bone & Joint Surgery(Br)* 1997; 79B (Suppl 1): 98

Patchell RA, Tibbs PA, Regine WF, et al. Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial. *The Lancet* 2005; 366(9486);643 – 648

Pazonis TJ1, Papanastassiou ID, Maybody M, Healey JH. Embolization of Hypervascular Bone Metastases Reduces Intraoperative Blood Loss: A Case-control Study. *Clin Orthop Relat Res.* 2014 Oct;472(10):3179-87. doi: 10.1007/s11999-014-3734-3. Epub 2014 Jun 26.

Peddi, P., Lopez-Olivo, M. A., Pratt, G. F., & Suarez-Almazor, M. E. (2013). Denosumab in patients with cancer and skeletal metastases: a systematic review and meta-analysis. *Cancer treatment reviews*, 39(1), 97-104.

Phillips CD et al. Nontraumatic avulsion of the lesser trochanter: a pathognomonic sign of metastatic disease? *Skeletal Radiology* 1998; 17(2); 106-110

Ratasvuori, M., Wedin, R., Keller, J., et al. (2013). Insight opinion to surgically treated metastatic bone disease: Scandinavian Sarcoma Group Skeletal Metastasis Registry report of 1195 operated skeletal metastasis. *Surgical oncology*, 22(2), 132-138.

Ratasvuori M1, Wedin R, Hansen BH, Keller J, Trovik C, Zaikova O, Bergh P, Kalen A, Laitinen M. Prognostic role of en-bloc resection and late onset of bone metastasis in patients with bone-seeking carcinomas of the kidney, breast, lung, and prostate: SSG study on 672 operated skeletal metastases. *J Surg Oncol.* 2014 Sep;110(4):360-5. doi: 10.1002/jso.23654. Epub 2014 May 29.

Ross JR, Saunders Y, Edmonds PM et al. A systematic review of the role of bisphosphonates in metastatic disease. *Health Technology Assessments* 2004;8:1-176.

Schiavon G, Tait DM, Briggs TW, Smith IE. A solitary bone lesion in a patient with previous breast cancer and the importance of bone biopsy: a case report and a review of guidelines. *Clin Breast Cancer.* 2013 Feb;13(1):77-80. doi: 10.1016/j.clbc.2012.10.004. Epub 2012 Nov 29.

Sharma H, Bhagat S, McCaul J, Macdonald D, Rana B, Naik M (2007). Intramedullary nailing for pathological femoral fractures. *Journal of Orthopaedic Surgery* (2007), 15(3).

Sørensen, M. S., Gregersen, K. G., Grum-Schwensen, T., Hovgaard, D., & Petersen, M. M. (2013). Patient and implant survival following joint replacement because of metastatic bone disease: A cross-sectional study of 130 patients with 140 joint replacements. *Acta orthopaedica*, 84(3), 301-306.

Steensma M, Boland PJ, Morris CD, Athanasian E, Healey JH. Endoprosthetic Treatment is More Durable for Pathologic Proximal Femur Fractures. *Clinical Orthopedics & Related Research* (2012) 470:920–926

Steensma, M., & Healey, J. H. (2013). Trends in the surgical treatment of pathologic proximal femur fractures among Musculoskeletal Tumor Society members. *Clinical Orthopaedics and Related Research*®, 471(6), 2000-2006.

Storm HH, Kejs AMT, Engholm G, Tryggvadóttir L, Klint Å, Bray F, Hakulinen T (2010). Trends in the overall survival of cancer patients diagnosed 1964-2003 in the Nordic countries followed up to the end of 2006: the importance of case-mix. *Acta Oncologica*, 49(5), 713-724.

Tillman R M. The Role of the Orthopaedic Surgeon in Metastatic Disease of the Appendicular Skeleton - Editorial. *Journal of Bone and Joint Surgery*, (Br) 1999: 81 - B: 1-2.

Tillman, R. M., Myers, G. J. C., Abudu, A. T., Carter, S. R., & Grimer, R. J. (2008). The three-pin modified 'Harrington' procedure for advanced metastatic destruction of the acetabulum. *Journal of Bone & Joint Surgery, British Volume*, 90(1), 84-87.

Tokuhashi Y, Matsuzaki H, Oda H, Oshima M, Ryu J. A revised scoring system for preoperative evaluation of metastatic spine tumor prognosis. *Spine* 2005; 30: 2186–91.

Tomita K, Kawahara N, Kobayashi T, Yoshida A, Murakami H, Akamura T. Surgical strategy for Spinal Metastasis *Spine* 2001: 26:298

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

Townsend PW, Smalley SR, Cozad SC, Rosenthal HG, Hassanein RES. Role of postoperative radiation therapy after stabilization of fractures caused by metastatic disease. *International Journal of Radiation Oncology Biology Physics* (1995);31(1):43 -49

Vakaet LA, Boterberg T. Pain control by ionizing radiation of bone metastasis *International Journal of Developmental Biology* 2004: 48: 599-606

Wedin R, Bauer H, Wersall P. Failures after operation for Skeletal Metastases of long bones. *Clinical Orthopedics & Related Research* 1999; 358: 128-139.

Wedin R, Hansen BH, Laitinen M, Trovik C, Zaikova O, Bergh P, Kalén A, Schwarz-Lausten G, Vult von Steyern F, Walloe A, Keller J, Weiss RJ. Complications and survival after surgical treatment of 214 metastatic lesions of the humerus. *J Shoulder Elbow Surg.* 2012 Aug;21(8):1049-55. doi: 10.1016/j.jse.2011.06.019. Epub 2011 Oct 7.

Weiss, K. R., Bhumbra, R., Biau, D. J., Griffin, A. M., Deheshi, B., Wunder, J. S., & Ferguson, P. C. (2011). Fixation of pathological humeral fractures by the cemented plate technique. *Journal of Bone & Joint Surgery, British Volume*, 93(8), 1093-1097.

Weiss, R. J., Ekström, W., Hansen, B. H., Keller, J., Laitinen, M., Trovik, C., ... & Wedin, R. (2013). Pathological subtrochanteric fractures in 194 patients: A comparison of outcome after surgical treatment of pathological and non-pathological fractures. *Journal of surgical oncology*, 107(5), 498-504.

Weiss, R. J., Tullberg, E., Forsberg, J. A., Bauer, H. C., & Wedin, R. (2014). Skeletal metastases in 301 breast cancer patients: Patient survival and complications after surgery. *The Breast*, 23(3), 286-290.

Whitehouse S, Stephenson J, Sinclair V, et al. A validation of the Oswestry Spinal Risk Index. *European Spine Journal*, (2014). 1-5.

Wibmer C, Leithner A, Hofmann G, *et al.* Survival analysis of 254 patients after manifestation of spinal metastases - evaluation of seven preoperative scoring systems. *Spine* 2011. doi:10.1097/BRS.0b013e3182011f84.