

*London Cancer*  
**Guidelines for Myeloma**

June 2014

## 1. Introduction

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These guidelines are intended to direct the treatment of patients with Myeloma; Solitary Bone Plasmacytoma and Solitary Extramedullary Plasmacytoma with radiotherapy. They have been developed from guidelines already in existence at Barts Health NHS Trust, University College London Hospitals NHS Foundation Trust, Royal Free London NHS Foundation Trust, Princess Alexander Hospital, North Middlesex Hospital and Barking, Havering and Redbridge University Hospitals NHS Trust. They should be read and used in conjunction with other guidelines covering the investigation and management of Myeloma. They also do not remove the need to follow the Local Rules and Work Instructions that have been developed at individual radiotherapy departments

## 2. Multiple Myeloma

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- Treatment decisions in multiple myeloma are guided by symptoms and evidence of myeloma-related organ or tissue impairment. The International Myeloma Working group has provided guidance to identify those patients with symptomatic myeloma as detailed in the London Cancer Guidelines for the Treatment of Multiple Myeloma.
- Mainstay of treatment is with systemic therapy
- Role of radiotherapy is for palliation of symptomatic lesions.

### 2.1. INDICATIONS and INTENT

Palliative Intent e.g.

- Symptom control of painful lesion
- spinal cord compression; cranial nerve or peripheral nerve compression
- impending or actual pathological fracture (high risk lesions to be considered for surgical stabilisation with post-operative radiotherapy to improve pain and local control).

### 2.2. TIMING

- Radiotherapy to start 2 weeks from time of decision to treat.
- Palliation falls into Category 3 patients

Radiotherapy Dose schedules

- 10-30Gy in 5-10 fractions
- 4-8 Gy single fraction

### 2.3. CHEMOTHERAPY AND EBRT

Chemotherapy schedules are covered in the London Cancer Guidelines for the Treatment of Multiple Myeloma document.

### 2.4. ESSENTIAL INVESTIGATIONS AND INFORMATION REQUIRED PRIOR TO DECISION TO TREAT FOR EBRT

The following investigations should have been performed and the results available before planning commences:

- Clinical history
- Baseline clinical examination and Performance Status
- All patients should have a histological diagnosis
- Staging investigations include FBC, U+E's and biochemical profile, Myeloma screen, Skeletal survey, CT/MRI of relevant site as appropriate e.g. for spinal cord compression.
- Consent form to be signed before planning.

## 2.5. INFORMATION FOR PATIENTS

Patients should be given an appropriate patient information leaflet about their treatment and have access to a myeloma nurse clinical nurse specialist or other specialist practitioner.

## 2.6. CONSENT

All patients must have given written informed consent before radiotherapy planning commences. Consent is to be taken by a practitioner who is familiar with myeloma radiotherapy planning and administration.

## 2.7. TRIALS

- RIC UCBT - Transplantation of umbilical cord blood from unrelated donors in patients with haematological diseases using a reduced intensity conditioning regimen

## 2.8. POSITION / IMMOBILISATION

- Dependent on site of lesion to be treated
- As that for bone metastasis at the affected site with most expected to be planned and treated in the supine position.
- Appropriate immobilization for the site being treated is required.

## 2.9. VOLUME DELINEATION AND NOMENCLATURE

GTV – Gross tumour volume

CTV – Clinical Target volume

PTV – Planning target volume

Margins applied dependent on site and treatment modality utilised.

As with other palliative cases, the treatment volume may instead be defined by treatment field border, ensuring sufficient margin from the GTV. Beneficial in the re-treatment setting where matching of field borders may be required.

## 2.10. IMAGE ACQUISITION / PLANNING / TECHNIQUE

Clinical mark-up, e.g. in treatment of rib lesions

Simulator / virtual simulator mark-up

3D planning using CT data for more complex cases

## 2.11. TREATMENT TECHNIQUE

Simple beam arrangements are often used.

Conformal plan with field arrangements devised according to treatment site and complexity of case.

Orthovoltage or electrons considered to treat rib lesions, otherwise MV photons

## 2.12. TREATMENT VERIFICATION

Linac Verification +/- image guidance as appropriate

## 2.13. ON TREATMENT REVIEW DEFINITION AND FOLLOW-UP

Weekly review for assessment and documentation of toxicity

Dependent on site irradiated:

- Lethargy
- Dysphagia if cervical or thoracic spine irradiated
- Dry mouth if cervical spine
- Diarrhoea and nausea with thoracic, lumbar spine and pelvis

## Follow up

- OPA 4-6 weeks following completion of radiotherapy
- Thereafter follow-up may continue under the relevant haematology team

## 3. Solitary Bone Plasmacytoma (SBP)

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Most commonly affect the axial skeleton, especially the vertebra

- Single area of bone destruction associated with clonal plasma cells
- Normal bone marrow aspirate and trephine
- Otherwise normal skeletal survey
- No anaemia, immune paresis, hypercalcaemia or renal impairment secondary to plasma cell dyscrasia
- Absent or low level serum paraprotein or urinary light chains
- No additional lesions on MRI spine
- Histology with pathological review by a histopathologist with special interest in bone or lymphoproliferative disorders. Monoclonality and/or an aberrant plasma cell phenotype must be demonstrated.

### 3.1. INDICATIONS and INTENT

- Radical intent

### 3.2. TIMING

- Radiotherapy to start within 4 weeks from time of decision to treat.
- Category 2 patients

### 3.3. ESSENTIAL INVESTIGATIONS AND INFORMATION REQUIRED PRIOR TO DECISION TO TREAT FOR EBRT

- Histological diagnosis required
- Staging investigations include FBC, Myeloma screen, Bone marrow aspirate and trephine, skeletal survey, MRI of whole spine and pelvis and CT/MRI of affected site to delineate lesion. CT/PET has the advantage of imaging the whole body and as such may identify other lesions (especially extramedullary) not seen on MRI. However it remains investigational and is not yet validated as a mandatory part of SBP staging.
- Urgent Neurosurgical review if concern regards spinal stability and /or neurological compromise. Should surgery be required this should precede radiotherapy.
- If lumbar-sacral site offer male patient sperm banking and female patient option of repositioning of ovaries or storing ovum or fertilized eggs if fertility at risk.
- Consent form to be signed before planning.

### 3.4. INFORMATION FOR PATIENTS

Patients should be given an appropriate patient information leaflet about their treatment and have access to a myeloma nurse clinical nurse specialist or other specialist practitioner.

### 3.5. CONSENT

All patients must have given written informed consent before radiotherapy planning commences. Consent is to be taken by a practitioner who is familiar with myeloma radiotherapy planning and administration.

### 3.6. TRIALS

- RIC UCBT - Transplantation of umbilical cord blood from unrelated donors in patients with haematological diseases using a reduced intensity conditioning regimen

### 3.7. POSITION / IMMOBILISATION

- Position and immobilisation devices used dependent on site of lesion to be treated and mobility of patient.
- Thoraco-lumbar Spinal SBP often treated prone with wedged pair beam arrangement
- Cervical spine SBP – immobilization with thermoplastic shell

### 3.8. IMAGE ACQUISITION

- Patients are 3D-planned using data from a CT planning scan.
- Contiguous slices with slice thickness of no more than 3mm taken through the region of interest.

### 3.9. VOLUME DELINEATION AND NOMENCLATURE

Consider MRI fusion for spinal SBP. CT and MRI to determine Gross Tumour volume (GTV)

CTV= Clinical Target Volume:

- Non-spinal SBP:
  - CTV=GTV+1.5-2cm (to cover microscopic disease, excluding barriers to extension of local disease e.g. muscle).
- Spinal SBP
  - superior and inferior field borders to include one normal vertebral body above and below the GTV
  - CTV = involved vertebra except where extraosseous involvement where same principles as for non-spinal SBP applies
  - Avoid kidneys in field.

PTV = Planning Target Volume

PTV=CTV+0.5-1cm (depending on immobilization technique utilized, to account for geometric moments and positional uncertainties)

Organs at risk (OAR)

- Solitary spinal plasmacytoma:
  - spinal cord – 42Gy (for 40Gy/20#) - 46Gy (when treating at 2Gy per fraction)
- Other sites:
  - OAR depends on site treated with standard constraints for that OAR. Refer to London Cancer Clinical Guidelines for Lymphoma for table with suggested constraints.

### 3.10. PLANNING TECHNIQUE

3D planning using CT data

### 3.11. TREATMENT TECHNIQUE

Conformal plan with field arrangements devised according to treatment site.

Field arrangement dependent on site treated.

Consider posterior oblique wedged pair fields for thoraco-lumbar vertebrae sites.

IMRT may be found beneficial for certain sites close to OAR

### 3.12. DOSE

Solitary Bone Plasmacytoma <5cm diameter: 40-45Gy in 20-25fractions, 2Gy per fraction

Solitary Bone Plasmacytoma >5cm diameter: 45-50Gy in 25 fractions; 1.8-2Gy per fraction

### 3.13. TREATMENT VERIFICATION

Linac Verification

Image guided verification desirable particularly for sites adjacent to critical dose limiting OAR e.g daily kV imaging with bone match and correction

### 3.14. ON TREATMENT REVIEW DEFINITION AND SCHEDULE GAP CATEGORY FOR MANAGEMENT OF UNSCHEDULED INTERRUPTIONS

Weekly review for assessment and documentation of toxicity

Weekly FBC if spinal site

Toxicity - according to site and extent of OAR exposure.

All toxicities to be explained to the patient at time consent obtained.

### 3.15. FOLLOW-UP

- Follow-up in clinic in 4-6 weeks and thereafter they may under the relevant haematology team.
- Consider evaluation for response with MRI at 8 weeks
- If no response to radiotherapy consider for chemotherapy as for myeloma including consolidation with high dose therapy for suitable patients.
- Relapse may take the form of a new solitary lesion at a different site. Radical radiotherapy to this new site of disease may be considered so deferring chemotherapy until clear evidence of myeloma

## 4. Solitary Extramedullary Plasmacytoma (SEP)

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Less common than SBP but carry a better prognosis

>90% arise in head and neck ( nasopharynx/ nasal sinuses/ oropharynx/ salivary glands/ larynx) but may occur almost anywhere in the body

- Single extramedullary mass of clonal plasma cells
- Normal bone marrow aspirate and trephine
- Normal skeletal survey
- No anaemia, immune paresis, hypercalcaemia or renal impairment secondary to plasma cell dyscrasia
- Absent or low level serum paraprotein or urinary light chains
- MRI not required – does not detect further occult disease
- CT/PET may identify other asymptomatic lesions but its role in routine work-up is not yet clear
- Histology with pathological review by a histopathologist with special interest in bone or lymphoproliferative disorders. Monoclonality and/or an aberrant plasma cell phenotype must be demonstrated

### 4.1. INDICATIONS and INTENT

- Radical intent
- Surgical excision to be considered where minimal morbidity and may be required for diagnosis. If margins are complete post-operative radiotherapy is not required. (Soutar et al 2004)
- Post-operative Radiotherapy for positive margins

- As primary treatment for SEP where surgery not feasible or associated with significant morbidity
- Coverage of primary echelon nodes if primary disease is a lymphatic structure (lymph nodes, Waldeyer's ring) remains controversial with reports of low regional node failure when not included in target volume. (Harwood et al, 1981, Knowling et al, 1983, Mayr et al, 1990, Strojjan et al, 2002)

#### 4.2. TIMING

- Radiotherapy to start within 4 weeks from time of decision to treat.
- Category 2 patients

#### 4.3. ESSENTIAL INVESTIGATIONS AND INFORMATION REQUIRED PRIOR TO DECISION TO TREAT FOR EBRT

- Histological diagnosis required
- Staging investigations include FBC, Myeloma screen, Bone marrow aspirate and trephine, skeletal survey, MRI CT/MRI of affected site to delineate lesion and assess for local nodal involvement (observed in approximately 10-20% of cases at presentation).
- CT/PET has the advantage of imaging the whole body and as such may identify other lesions (especially extramedullary) not seen on MRI. However it remains investigational and is not yet validated as a mandatory part of SBP staging.
- If pelvic site offer male patient sperm banking and female patient option of repositioning of ovaries or storing ovum or fertilized eggs if fertility at risk.
- Consent form to be signed before planning.

#### 4.4. INFORMATION FOR PATIENTS

Patients should be given an appropriate patient information leaflet about their treatment and have access to a myeloma nurse clinical nurse specialist or other specialist practitioner.

#### 4.5. CONSENT

All patients must have given written informed consent before radiotherapy planning commences. Consent is to be taken by a practitioner who is familiar with myeloma radiotherapy planning and administration.

#### 4.6. TRIALS

- RIC UCBT - Transplantation of umbilical cord blood from unrelated donors in patients with haematological diseases using a reduced intensity conditioning regimen

#### 4.7. POSITION / IMMOBILISATION

- Position and immobilisation devices used dependent on site of lesion to be treated and mobility of patient.
- Head and neck sites – immobilization with thermoplastic shell with appropriate neck position for head and neck site to be treated.

#### 4.8. IMAGE ACQUISITION

- Patients are 3D-planned using data from a CT planning scan.
- Contiguous slices with slice thickness of no more than 3mm taken through the region of interest.
- i.v. contrast to be considered e.g. head and neck sites; nodal involvement

## 4.9. VOLUME DELINEATION AND NOMENCLATURE

CTV= Clinical Target Volume:

- CTV=GTV+1.5-2cm (to cover microscopic disease, excluding barriers to extension of local disease).
- Local nodal chain to be included in CTV only if clinically involved

PTV=CTV+0.5-1cm (depending on immobilization technique utilized, to account for geometric moments and positional uncertainties)

Organs at risk (OAR)

OAR depends on site treated with standard constraints for that OAR. Refer to London Cancer Clinical Guidelines for Lymphoma for table with suggested constraints.

## 4.10. PLANNING TECHNIQUE

3D planning using CT data

## 4.11. TREATMENT TECHNIQUE

Conformal plan with field arrangements devised according to treatment site.

Field arrangement dependent on site treated.

IMRT may be found beneficial for head and neck sites

## 4.12. DOSE

SEP <5cm diameter: 40-45Gy in 20-25fractions, 2Gy per fraction

SEP >5cm diameter: 45-50Gy in 25 fractions; 1.8-2Gy per fraction

## 4.13. TREATMENT VERIFICATION

Linac Verification

Image guided verification to be considered and required for head and neck sites

e.g daily kV imaging with bone match and correction

## 4.14. ON TREATMENT REVIEW DEFINITION AND SCHEDULE GAP CATEGORY FOR MANAGEMENT OF UNSCHEDULED INTERRUPTIONS

Weekly review for assessment and documentation of toxicity

For head and neck sites –care on treatment as per solid tumour affecting that site (refer to London Cancer Radiotherapy Guidelines for Head and neck malignancies)

Toxicity - according to site and extent of OAR exposure.

All toxicities to be explained to the patient at time consent obtained.

## 4.15. FOLLOW-UP

- Follow-up in clinic in 4-6 weeks and thereafter they may under the relevant haematology team.
- Consider imaging evaluation for response at 8 weeks
- Adjuvant chemotherapy may be considered for lesions >5cm or those of high grade although its role remains uncertain