Pros and cons of different imaging techniques, focused on MRI and 18-F FDG PET/CT, in the evaluation of Multiple Myeloma

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Learning objectives

To show the role of the different techniques in the diagnosis and monitoring of Multiple (MM), focused on whole body magnetic resonance (MRI) and $^{18}$FDG-PET/CT.

To describe the advantages and limitations of each technique to diagnose this illness.

To illustrate the spectrum of musculoskeletal pathologies and complications in patients with MM.

Background

MM is an incurable hematologic malignancy, the second most common after non-Hodgkin lymphoma, characterized by clonal proliferation of mature plasma cells and overproduction of monoclonal immunoglobulins\(^1\).

MM is more prevalent in African descendants and slightly more common in men. The median age at diagnosis is 70 years with an incidence of 5,6 cases/100 000 people/ year\(^2\).

Anemia is the most common clinical feature of this illness. Bone pain, renal insufficiency, fatigue, weight loss and hypercalcemia can also be found.

The diagnosis of MM is based on multiple parameters (clinical, analytical and anatomical and functional based modalities imaging) established in different classifications such as the Durie Salmon Staging (DSS) System, the Plus DSS and the International Myeloma Working Group (IMWG). The radiologist must know these to make an accurate diagnosis that may change the management of the patient.

The DSS Plus classification includes for the first time the number of focal lesions of 5 mm or larger and the pattern observed at MRI or $^{18}$FDG PET/CT in the staging. Table 1 on page 3
In this abstract we will explain the different imaging techniques available to manage this illness, focussed on the role of the whole body MRI and the $^{18}$FDG-PET/CT in the diagnosis, initial staging, evaluation of the response to treatment and complications.

Images for this section:

<table>
<thead>
<tr>
<th>Classification</th>
<th>Whole-body MRI and/or FDG-PET</th>
</tr>
</thead>
<tbody>
<tr>
<td>MGUS</td>
<td>All negative</td>
</tr>
<tr>
<td>Stage IA</td>
<td>Normal skeletal survey or single lesion (smoldering)</td>
</tr>
<tr>
<td>Stage IB</td>
<td>&lt; 5 focal lesions or mild diffuse disease</td>
</tr>
<tr>
<td>Stage II A/B</td>
<td>5-20 focal lesions or moderate diffuse disease</td>
</tr>
<tr>
<td>Stage III A/B</td>
<td>&gt; 20 focal lesions or severe diffuse disease</td>
</tr>
</tbody>
</table>

**Table 1:** Durie Salmon Plus staging system. This modified version of the Durie Salmon staging system includes imaging information which consists on the number of focal lesions with 5 mm or more in size and the extent of diffuse bone marrow disease seen at MR imaging or FDG PET/CT. MGUS: monoclonal gammopathy of undetermined significance. Stage A: Normal renal function. Stage B: Abnormal renal function.

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Findings and procedure details

Up to 90% of the patients with MM will develop osteolytic lesions \(^{(3)}\), in the course of the disease. It is important to have a diagnostic algorithm that help us to determinate the extension of the disease, the presence of intra and extramedullary involvement, the response to treatment and the appearance of complications.

**Skeletal survey (SS).**

Conventional radiography is the imaging technique of choice in the initial diagnosis of MM and is still considered the "Gold Standard" to determinate the extent of MM.

It has great accuracy to detect osteolytic lesions, especially those located in skull. Fig. 1 on page 8

In our center we include anteroposterior views of the thorax, cervical, dorsal and lumbar spine, pelvis, upper and lower extremities and lateral views of the skull, cervical, dorsal and lumbar spine.

Lytic lesions appear as punched-out holes without surrounding reactive sclerosis that represent the bone destruction and replacement of the bone marrow with tumoral cells (plasma mature cells) \(^{(4)}\). Fig. 2 on page 9

SS has some disadvantages: it misses 20% of lytic lesions Fig. 3 on page 10 , does not detect variegated/diffuse bone marrow infiltration Fig. 4 on page 10 , has low specificity in the diagnosis of benign causes of osteopenia such as those related to postmenopausal or steroid treatment and finally, does not show changes after the response to treatment. Fig. 5 on page 11

Due to the limitations of the SS and the introduction of new anatomical and functional imaging techniques, the use of MRI, FDG-PET/CT and CT has been increasing.

**CT.**

CT has a higher sensibility and specificity than SS to detect small lesions in some locations. Fig. 6 on page 12
Other advantages are the detection of soft tissue involvement and the option to perform 3D reconstructions Fig. 7 on page 12, and to realize CT-guided biopsies to plan surgery or radiotherapy.

MM lesions seen in CT do not disappear after treatment and that is a potential source of errors in the evaluation of the disease. Fig. 8 on page 13

**MRI.**

We perform whole-body and whole spine MRI in a 1.5 T General Electric magnet. We realize coronal T1-weighted (turbo spin-echo) and STIR sequences from head to ankles and sagittal T1-weighted and STIR sequences of the entire spine with post-processing imaging pasting in both cases. We complete the study with diffusion sequences.

IV contrast is only administrated in some patients with normal renal function and unsuspected diagnosis of MM.

Axial scanning ranges to cover a field of view from head to ankles.

First, the chest and abdomen are scanned with T1-weighted (turbo spin-echo) and STIR sequences. Sagittal scanning ranges to cover the entire spine in the same T1-weighted and STIR sequences.

According to the 2009 IMWG, MRI is very useful in patients with negative SS (20% of false negatives) and classic symptoms of the illness or in patients with suspected solitary plasmocitoma Fig. 9 on page 15 (4), also some publications advocates the use of MRI for routine staging, prognosis and assessment of response to treatment (5).

MM has different patterns of bone marrow involvement: normal marrow, micronodular pattern (also termed variegated or salt-and-pepper) and focal and diffuse pattern (6) Fig. 10 on page 15.

MRI detects bone marrow infiltration before bone destruction and it is more sensitive than the $^{18}$FDG-PET/CT in this location. Fig. 11 on page 16.

MRI is the imaging technique of choice in cord compression suspicion and establishes its location and extension. Fig. 3 on page 10. MRI is also useful to evaluate response to treatment Fig. 12 on page 17 and possible complications. The drawback is that in many cases it is unspecific and imaging findings are similar to those in inflammatory or
other tumoral diseases Fig. 13 on page 18. MRI signal abnormalities in MM persist up to five years’ after recovery.

We remind that this imaging technique is not possible to accomplish in patients with pacemakers, renal insufficiency or claustrophobia and the long acquisition time.

**18 FDG PET/CT:**

We perform hole-body CT covering a region ranging from the head to the upper thighs. PET images are acquired 60 minutes following the administration of 350 MBq of FDG covering the same field of view as CT.

18 FDG PET/CT has many advantages; provides reliable information to help detect early bone involvement Fig. 14 on page 19 like progression of stable monoclonal gammopathy of undetermined significance (MGUS) and smoldering multiple myeloma (SMM) which typically are negative in 18 FDG PET/CT images (7).

18 FDG PET/CT can detect and distinguish between intramedullary and extramedullary lesions Fig. 15 on page 20 in a single examination in patients with MM (8), makes an accurate diagnosis and stratify the extension of the bone marrow affection Fig. 16 on page 21 on the basis of 18 FDG uptake of the tissues.

18 FDG PET/CT predicts the illness prognosis better than other imaging techniques such as MRI or SS.

It also has been found to be more sensitive in treatment assessment Fig. 17 on page 21, the diagnostic of recurrence or progression than SS in patients treated with autologous stem cell transplantation Fig. 18 on page 22 and also is faster in the normalization of imaging finding than MRI does.

**Use of MRI and 18 FDG PET/CT together:**

The combination of 18 FDG PET/CT and whole-body MRI was found to have 100% specificity in the staging and posttreatment compared with the specificities of these techniques separately that are of 75% for 18 FDG PET/CT and 84% for MRI (9).
$^{18}$FDG PET/CT can be more accurate than MRI for detecting extramedullary disease but has low specificity about the $^{18}$FDG avidity of the tissues what can lead to false positives Fig. 19 on page 23 and may lead to false negatives in subcentimeter lesions overall those located in the skull (10).

MRI is a better imaging technique than $^{18}$FDG PET/CT for the evaluation of the axial skeleton and neurologic complications but had limitations to detect the peripheral affection, chiefly in the ribs or sternum. Fig. 20 on page 23

Complications:

Once the diagnosis and staging of patients with MM is established, it is very important to take into account the possible complications that these patients may have due to the immunosuppression that the treatments they receive can cause them.

Among these complications we present some common examples that we can find frequently and that can cause misdiagnosed.

Complications Fig. 21 on page 24:

· Pathological fractures: MM patients are normally elderly patients with osteopenia and the toxicity of the treatments they take can increase the possibilities of pathological fractures.

· Osteomyelitis: Bone infections can occur in patients with MM. The bone marrow signal can be affected with similar characteristics as in MM so many times differential diagnosis is made by pathological examination realized by puncture or surgery.

· Osteonecrosis: Osteopenia and diverse treatments can lead to different types of osteonecrosis. The most common type is osteonecrosis avascular of the femur or humerus and mandibular osteonecrosis due to bisphosphonates treatment.

Images for this section:
Table 2: Advantages and disadvantages of the different images modalities in the diagnosis and monitoring of MM.

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Fig. 1: A. 65 years old woman who presents a growing mass in her frontal part of the head. Lateral skull view shows a big osteolytic lesion (circle) with cortical destruction and soft tissue mass. The diagnosis of MM was established after biopsy and anatomo-pathological approach. B. 68 years old woman with diagnosis of MM. AP skull view shows multiple small lytic lesions (arrow).

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Fig. 2: 77 years old man with diagnosis of MM. Right ribs and right upper extremity view (A) shows an expansive and aggressively lesion in the distal third of the right clavicle with cortical rupture (circle), a lesion in the scapula is also seen. Pathological fracture with associated lesion from MM affects the diaphysis of the right humerus (arrow).
Multiple expansive lesions are seen in the right ribs (circle). AP Pelvis view (B) shows an expansive lesion in the right ischio-pubic region (circle).

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**Fig. 3:** Dorsal (A) and lumbar (B) lateral spine radiographies. No bone affection is seen. Whole column STIR MRI image (C) shows multiple bone affection in cervical, dorsal and lumbar levels (circles). Dorsal column STIR sequence (D) shows medullar compression and posterior elements affection (arrow). Lumbar column STIR sequence (E) shows a prevertebral mass and compression of the vertebral canal (arrow).

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Fig. 4: 70 years old woman with MM. Skeletal survey if performed. Images form the skeletal survey (AP pelvis (A), lateral dorsal (D) and lateral lumbar (E) spine views) do not show lytic lesions. T1 weighted (B) and STIR (C) coronal MRI images of the pelvis, T1 weighted (F) and STIR (G) sagittal lumbar spine MRI images show an extent infiltration of the bone marrow with a variegated pattern affection not visualized in the SS.

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**Fig. 5:** 50 years old man with MM diagnosed in 2004. Posteroanterior thorax view done after diagnoses shows an expansive and lytic lesion affecting the distal third of the right clavicle (circle). Chemotherapy reservoir is seen in right hemithorax. Posteroanterior thorax view done in September 2015. The patient is clinically and analytically in total relapse but the clavicle lesion persists but presents extensive sclerosis (circle).

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**Fig. 6:** 61 years old patient with MM treated with good response. The patient presents cervical pain resistant to analgesia. Sagittal (A), coronal (B) and axial (C) CT images show a lytic lesion (arrows) with cortical rupture which affects the cervical body of C2 with final diagnosis of MM. Degenerative changes and lost of intersomatical space are also seen affecting C5 and C6 and diffuse osteopenia.

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**Fig. 7:** 77 years old male (same patient as image 2). Axial CT images (A and B) show multiple lytic lesions (circles) affecting the ribs with soft tissue masses associated. 3D reconstructions image (C) shows lytic lesions affecting multiple ribs and the left scapula (circles).

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Fig. 8: 49 years old man who inquires about fatigue, poliarticular pain and a left supraclavicular mass. Axial CT image (A) at initial diagnose shows an expansive lesion with blastic and lytic components with soft tissue mass associated and cortical rupture in the first left rib with result of plasmocitoma after FNA (Fine needle aspiration). Axial CT image (B), years after treatment and in partial relapse, the lesion persists but has abundant sclerosis and there is no soft tissue mass associated.
Fig. 9: Plasmocitomas: Same patient from image 1A. Coronal T2-weighted image (A) and gadolinium-enhanced fat suppressed axial T1-weighted (B) images show a frontal plasmocitoma as a big osteolytic lesion with cortical destruction and soft tissue mass. 75 years old man with back pain. Axial CT image (C) and fat-saturated sagittal T1-weighted sequence after gadolinium administration (D) show a mass that affects a large part of the sacrum and extends from facet joints of L5 to coccygeal region and associates an intraspinal soft tissue mass, with an heterogeneous contrast enhancement.
**Fig. 10:** Different specific patterns of bone marrow involvement in MM. A. Normal signal. STIR whole column pasted images show no bone affection. B. Variegated or salt and pepper. T1 sagittal lumbar spine image shows an infiltration of the bone marrow with a variegated pattern affection. C. Focal. Multiple focal lesions in thoracic and lumbar spine hyperintense in sagittal whole column STIR sequence. D. Diffuse. Multiple hyperintense foci of the spine in sagittal whole column STIR sequence.

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Fig. 11: 59-year-old man with MM in treatment. The patient refers left hip pain. Fat-suppressed coronal T1-weighted sequence after gadolinium administration (A) shows bone marrow enhancement of the left acetabulum, left femoral head and neck related to MM infiltration without producing cortical rupture (circle). Subchondral hipointense femoral head collapse is seen due to necrosis avascular.

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Fig. 12: A and B. 60 years old man with initial diagnosis of MM. Sagittal whole column STIR image (A) shows multiple lesions of the bone marrow and whole column sagittal STIR image (B) after treatment shows a great response with normal bone marrow signal. C and D. 54 years old man with MM. Sagittal dorsolumbar column STIR image (C) shows multiple hyperintense bone marrow lesions with diffuse affection. Same sequence MR image (D) after treatment; the bone lesions have disappeared.

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**Fig. 13:** 66 years old woman with MM. MRI signal affection is seen in the right sacral wing and iliac bone, hypointense in T1 weighted image (A) and hyperintense in coronal (B) STIR image. PET/CT (C and D) and CT (E) axial images show a sclerotic lesion without evidence of glucose avidity. AP result: Chronic osteomyelitis.

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Fig. 14: 56 years old woman with smoldering myeloma, presents lumbar pain resistant to analgesia. SS was negative. PET/CT and MR are performed. Coronal and sagittal views of PET(A and C) and fusion PET/CT (B and D) show diffuse bone marrow affection with intense activity of the axial and peripheral skeleton. The circles mark the sternum activity.

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Fig. 15: 75 years old woman with MM IIIA stage in total relapse after treatment. T1 weighted MRI (A), Axial fusion PET/CT images (B and C) and coronal PET images (D
and E) show lymph node recurrence in the right laterocervical chain and mediastinum lymphadenopathies, both with intense activity.

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**Fig. 16:** 59 years old woman with recent diagnosis of MM. PET/CT is performed to evaluate bone marrow affection. Axial CT (A, C and E) and fusion PET/CT (B, D and F) images show multiple bone marrow involvement with 18FDG activity. A plasmocitoma (circles) is also seen affecting both sacral wings with cortical rupture and soft tissue mass.

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Fig. 17: 37 years old woman with MM IIIB stage. PET (A) and fusion PET/CT axial (C) images show diffuse bone marrow infiltration affecting the sacral and iliac bones. PET (B) and fusion PET/CT axial (D) images after treatment show a great response with total relapse of the bone marrow affection seen in the previous images.

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**Fig. 18:** 48 years old woman with MM treated with autologous cell stem transplantation and in clinical total relapse. PET/CT is performed to control the multiple bone affection she had at diagnosis. PET (A) and fusion PET/CT (C) axial images at initial diagnosis show sternum and vertebrae avidity due to MM infiltration. PET (B) and fusion PET/CT (D) axial images performed after treatment show progression of the sternum and vertebrae infiltration which means the patient still had active illness and had not responded to treatment.

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**Fig. 19:** 48 years old man with MM in total relapse after autologous stem cell transplantation. Axial (A) and coronal (B) fusion PET/CT images show intense uptake of the third and fourth left ribs suspicious of MM infiltration. Axial CT image (C) demonstrate callus fractures in the ribs with 18FDG avidity. The patient admitted a recent thoracic trauma two months previous to the PET/CT.

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**Fig. 20:** Female patient with polyneuropathy, monoclonal gammopathy and negative SS. MRI and PET/CT were performed to detect possible bone affection. Coronal STIR image (A) shows multiple hyperintense foci in the left ribs suspicious for bone marrow infiltration. Coronal fusion PET/CT and CT images (B and C) show no abnormal glucose avidity in the bone marrow. The image from the MRI was a false positive due to an artifact and final diagnosis of POEMS syndrome was made in the patient.

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Fig. 21: Complications in patients with MM due to immunosuppression or osteopenia. A. Pathological fracture affecting L1 vertebrae is shown in sagittal MRI images of the spine as hypointense in T1, hyperintense in STIR and with intense enhancement in postcontrast sequence. B. CT axial image (same patient image 13) show a sclerotic lesion without evidence of activity. AP result: Chronic osteomyelitis. C and D. The partial collapse of the right femoral head, hypointense in coronal T1 weighted (C) and hyperintense in STIR (D) images demonstrates the avascular necrosis in a patient with MM and hip pain. E. Lytic lesion is seen in the AP ortopantomography view in patient with MM in treatment with bisphosphonates with final diagnose of osteonecrosis.

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Conclusion

Current guidelines still support the use of conventional radiography in all MM to detect bone affection. A multimodality imaging approach including other imaging techniques such as whole-body MRI and $^{18}$FDG-PET/CT are indicated specially in patients with normal SS and a monoclonal gammopathy or plasmocitoma.

MRI is also indicated in diffuse bone marrow infiltration and potential neurologic complications. PET/CT has a higher sensitivity and specificity in the evaluation of MM activity and treatment response.

Personal information

References


